# WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



# INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

C07H 21/04, C07K 14/705, C12N 15/09, A1 15/63, C12Q 1/68				
15/05, 012Q 1500	(43) International Publication Date: 2 March 2000 (02.03.00)			
(21) International Application Number: PCT/US99/19351 (22) International Filing Date: 24 August 1999 (24.08.99)	(74) Agent: SPRUNGER, Suzanne, A.; American Home Products Corporation, Patent & Trademark Dept. – 2B, One Campus Drive, Parsippany, NJ 07054 (US).			
(30) Priority Data: 60/097,638 24 August 1998 (24.08.98) 60/097,659 24 August 1998 (24.08.98) 60/099,618 9 September 1998 (09.09.98) 60/102,092 28 September 1998 (28.09.98) 60/109,978 25 November 1998 (25.11.98) 60/113,645 23 December 1998 (23.12.98) 60/113,646 23 December 1998 (23.12.98) 09/379,246 23 August 1999 (23.08.99) US  (71) Applicant: ALPHAGENE, INC. [US/US]; 260 West Cummings Park, Woburn, MA 01801 (US).  (72) Inventors: VALENZUELA, Dario; 260 West Cummings Park Woburn, MA 01801 (US). YUAN, Olive; 260 West Cummings Park, Woburn, MA 01801 (US). HOFFMAN Heidi; 260 West Cummings Park, Woburn, MA 01801 (US). HOFFMAN Heidi; 260 West Cummings Park, Woburn, MA 01801 (US). RAPIEJKO, Peter; 260 West Cumming Park, Woburn, MA 01801 (US).	GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  Published  With international search report.  Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.			

- (57) Abstract

Novel polynucleotides and the proteins encoded thereby are disclosed.

# FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	ТJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
ВJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	us	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

### SECRETED PROTEINS AND POLYNUCLEOTIDES ENCODING THEM

5

This application is a continuation-in-part of the following applications:

- (1) provisional application Ser. No. 60/097,638 (GI 6908), filed August 24, 1998;
- (2) provisional application Ser. No. 60/097,659 (GI 6909), filed August 24, 1998;
- (3) provisional application Ser. No. 60/099,618 (GI 6910), filed September 9, 1998;
- 10 (4) provisional application Ser. No. 60/102,092 (GI 6912), filed September 28, 1998;
  - (5) provisional application Ser. No. 60/109,978 (GI 6914), filed November 25, 1998;
  - (6) provisional application Ser. No. 60/113,645 (GI 6916), filed December 23, 1998; and
  - (7) provisional application Ser. No. 60/113,646 (GI 6917), filed December 23, 1998; all of which are incorporated by reference herein.

15

# FIELD OF THE INVENTION

The present invention provides novel polynucleotides and proteins encoded by such polynucleotides, along with therapeutic, diagnostic and research utilities for these polynucleotides and proteins.

20

25

35

# **BACKGROUND OF THE INVENTION**

Technology aimed at the discovery of protein factors (including e.g., cytokines, such as lymphokines, interferons, CSFs and interleukins) has matured rapidly over the past decade. The now routine hybridization cloning and expression cloning techniques clone novel polynucleotides "directly" in the sense that they rely on information directly related to the discovered protein (i.e., partial DNA/amino acid sequence of the protein in the case of hybridization cloning; activity of the protein in the case of expression cloning). More recent "indirect" cloning techniques such as signal sequence cloning, which isolates DNA sequences based on the presence of a now well-recognized secretory leader sequence motif, as well as various PCR-based or low stringency hybridization cloning techniques, have advanced the state of the art by making available large numbers of DNA/amino acid sequences for proteins that are known to have biological activity by virtue of their secreted nature in the case of leader sequence cloning, or by virtue of the cell or tissue source in the case of PCR-based techniques. It is to these proteins and the polynucleotides encoding them that the present invention is directed.

# **SUMMARY OF THE INVENTION**

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ IDNO:1;

10

15

20

25

30

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1 from nucleotide 683 to nucleotide 934;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vb11\_1 deposited with the ATCC under accession number 98846;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vb11\_1 deposited with the ATCC under accession number 98846;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vb11\_1 deposited with the ATCC under accession number 98846;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vb11\_1 deposited with the ATCC under accession number 98846;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:2;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:2;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above;
- (j) a polynucleotide which encodes a species homologue of the proteinof (g) or (h) above;
- (k) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h); and
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h) and that has a length that is at least 25% of the length of SEQ ID NO:1.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:1 from nucleotide 683 to nucleotide 934; the nucleotide sequence of the full-length

protein coding sequence of clone vb11\_1 deposited with the ATCC under accession number 98846; or the nucleotide sequence of a mature protein coding sequence of clone vb11\_1 deposited with the ATCC under accession number 98846. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vb11\_1 deposited with the ATCC under accession number 98846.

In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:2, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment comprising the amino acid sequence from amino acid 37 to amino acid 46 of SEQ ID NO:2.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:1.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:1, but excluding the poly(A) tail at the 3' end of SEQ ID NO:1; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vb11\_1 deposited with the ATCC under accession number 98846;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

10

20

25

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

5

10

15

20

25

30

(ba) SEQ ID NO:1, but excluding the poly(A) tail at the 3' end of SEQ ID NO:1; and

- (bb) the nucleotide sequence of the cDNA insert of clone vb11\_1 deposited with the ATCC under accession number 98846;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:1, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:1 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:1, but excluding the poly(A) tail at the 3' end of SEQ ID NO:1. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:1 from nucleotide 683 to nucleotide 934, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:1 from nucleotide 683 to nucleotide 934, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:1 from nucleotide 683 to nucleotide 934.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:2;
- (b) a fragment of the amino acid sequence of SEQ ID NO:2, the fragment comprising eight contiguous amino acids of SEQ ID NO:2; and
  - (c) the amino acid sequence encoded by the cDNA insert of clone vb11\_1 deposited with the ATCC under accession number 98846;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:2. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:2, or a protein comprising a fragment of the amino acid sequence of SEQ

ID NO:2 having biological activity, the fragment comprising the amino acid sequence from amino acid 37 to amino acid 46 of SEQ ID NO:2.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

5 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:3;

10

15

20

25

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:3 from nucleotide 63 to nucleotide 482;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:3 from nucleotide 201 to nucleotide 482;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vb12\_1 deposited with the ATCC under accession number 98846;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vb12\_1 deposited with the ATCC under accession number 98846;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vb12\_1 deposited with the ATCC under accession number 98846;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vb12\_1 deposited with the ATCC under accession number 98846;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:4;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:4;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:3.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:3 from nucleotide 63 to nucleotide 482; the nucleotide sequence of SEQ ID NO:3 from nucleotide 201 to nucleotide 482; the nucleotide sequence of the full-length protein coding sequence of clone vb12\_1 deposited with the ATCC under accession number 98846; or the nucleotide sequence of a mature protein coding sequence of clone vb12\_1 deposited with the ATCC under accession number 98846. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vb12\_1 deposited with the ATCC under accession number 98846. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:4, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4 having biological activity, the fragment comprising the amino acid sequence from amino acid 65 to amino acid 74 of SEQ ID NO:4.

10

15

25

30

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 20 ID NO:3.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:3, but excluding the poly(A) tail at the 3' end of SEQ ID NO:3; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vb12\_1 deposited with the ATCC under accession number 98846;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

5

10

15

20

25

30

and

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:3, but excluding the poly(A) tail at the 3' end of SEQ ID NO:3; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vb12\_1 deposited with the ATCC under accession number 98846;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:3, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:3 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:3, but excluding the poly(A) tail at the 3' end of SEQ ID NO:3. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:3 from nucleotide 63 to nucleotide 482, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:3 from nucleotide 63 to nucleotide 482, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:3 from nucleotide 63 to nucleotide 482. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:3 from nucleotide 201 to nucleotide 482, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:3 from nucleotide 201 to nucleotide 482, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:3 from nucleotide 201 to nucleotide 482.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:4;

(b) a fragment of the amino acid sequence of SEQ ID NO:4, the fragment comprising eight contiguous amino acids of SEQ ID NO:4; and

- (c) the amino acid sequence encoded by the cDNA insert of clone vb12\_1 deposited with the ATCC under accession number 98846;
- 5 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:4. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:4, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4 having biological activity, the fragment comprising the amino acid sequence from amino acid 65 to amino acid 74 of SEQ ID NO:4.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:5;

20

25

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:5 from nucleotide 1195 to nucleotide 1527;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:5 from nucleotide 1468 to nucleotide 1527;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vb14\_1 deposited with the ATCC under accession number 98846;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vb14\_1 deposited with the ATCC under accession number 98846;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vb14\_1 deposited with the ATCC under accession number 98846;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vb14\_1 deposited with the ATCC under accession number 98846;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:6;

5

10

15

20

25

- a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:6;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:5.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:5 from nucleotide 1195 to nucleotide 1527; the nucleotide sequence of SEQ ID NO:5 from nucleotide 1468 to nucleotide 1527; the nucleotide sequence of the full-length protein coding sequence of clone vb14\_1 deposited with the ATCC under accession number 98846; or the nucleotide sequence of a mature protein coding sequence of clone vb14\_1 deposited with the ATCC under accession number 98846. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vb14\_1 deposited with the ATCC under accession number 98846. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:6, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6 having biological activity, the fragment comprising the amino acid sequence from amino acid 50 to amino acid 59 of SEQ ID NO:6.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:5.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

PCT/US99/19351 WO 00/11015

(i)

preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of: (aa) SEQ ID NO:5, but excluding the poly(A) tail at the 5 3' end of SEQ ID NO:5; and (ab) the nucleotide sequence of the cDNA insert of clone vb14\_1 deposited with the ATCC under accession number 98846; hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and 10 isolating the DNA polynucleotides detected with the probe(s); and (b) a process comprising the steps of: preparing one or more polynucleotide primers that 15 hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of: SEQ ID NO:5, but excluding the poly(A) tail at the (ba) 3' end of SEQ ID NO:5; and the nucleotide sequence of the cDNA insert of clone 20 vb14\_1 deposited with the ATCC under accession number 98846; (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; (iii) amplifying human DNA sequences; and (iv) isolating the polynucleotide products of step (b)(iii). 25 Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:5, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:5 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:5, but excluding the poly(A) tail at the 3' end of SEQ ID NO:5. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the 30 cDNA sequence of SEQ ID NO:5 from nucleotide 1195 to nucleotide 1527, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:5 from nucleotide 1195 to nucleotide 1527, to a nucleotide sequence

corresponding to the 3' end of said sequence of SEQ ID NO:5 from nucleotide 1195 to

nucleotide 1527. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:5 from nucleotide 1468 to nucleotide 1527, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:5 from nucleotide 1468 to nucleotide 1527, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:5 from nucleotide 1468 to nucleotide 1527.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10

5

- (a) the amino acid sequence of SEQ ID NO:6;
- (b) a fragment of the amino acid sequence of SEQ ID NO:6, the fragment comprising eight contiguous amino acids of SEQ ID NO:6; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vb14\_1 deposited with the ATCC under accession number 98846;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:6. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:6, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6 having biological activity, the fragment comprising the amino acid sequence from amino acid 50 to amino acid 59 of SEQ ID NO:6.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

NO-7

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:7;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:7 from nucleotide 82 to nucleotide 294;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:7 from nucleotide 109 to nucleotide 294;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone ve11\_1 deposited with the ATCC under accession number 98846;

 (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone ve11\_1 deposited with the ATCC under accession number 98846;

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vel1\_1 deposited with the ATCC under accession number 98846;

5

10

15

20

25

- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone ve11\_1 deposited with the ATCC under accession number 98846;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:8;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:8;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:7.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:7 from nucleotide 82 to nucleotide 294; the nucleotide sequence of SEQ ID NO:7 from nucleotide 109 to nucleotide 294; the nucleotide sequence of the full-length protein coding sequence of clone ve11\_1 deposited with the ATCC under accession number 98846; or the nucleotide sequence of a mature protein coding sequence of clone ve11\_1 deposited with the ATCC under accession number 98846. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone ve11\_1 deposited with the ATCC under accession number 98846. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:8, or a polynucleotide

encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment comprising the amino acid sequence from amino acid 30 to amino acid 39 of SEQ ID NO:8.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 5 ID NO:7.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:7, but excluding the poly(A) tail at the 3' end of SEQ ID NO:7; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vell\_1 deposited with the ATCC under accession number 98846;
  - (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
  - (iii) isolating the DNA polynucleotides detected with the probe(s);
- 20 and

10

15

25

30

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:7, but excluding the poly(A) tail at the 3' end of SEQ ID NO:7; and
  - (bb) the nucleotide sequence of the cDNA insert of cloneve11\_1 deposited with the ATCC under accession number 98846;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:7, and extending

contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:7 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:7, but excluding the poly(A) tail at the 3' end of SEQ ID NO:7. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:7 from nucleotide 82 to nucleotide 294, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:7 from nucleotide 82 to nucleotide 294, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:7 from nucleotide 82 to nucleotide 294. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:7 from nucleotide 109 to nucleotide 294, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:7 from nucleotide 109 to nucleotide 294, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:7 from nucleotide 109 to nucleotide 294.

5

10

15

20

25

30

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:8;
- (b) a fragment of the amino acid sequence of SEQ ID NO:8, the fragment comprising eight contiguous amino acids of SEQ ID NO:8; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vell\_1 deposited with the ATCC under accession number 98846;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:8. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:8, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment comprising the amino acid sequence from amino acid 30 to amino acid 39 of SEQ ID NO:8.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:9;

5

10

15

20

25

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:9 from nucleotide 22 to nucleotide 468;

- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:9 from nucleotide 118 to nucleotide 468;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vf2\_1 deposited with the ATCC under accession number 98846;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vf2\_1 deposited with the ATCC under accession number 98846;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vf2\_1 deposited with the ATCC under accession number 98846;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vf2\_1 deposited with the ATCC under accession number 98846;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:10;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:10;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:9.
- Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:9 from nucleotide 22 to nucleotide 468; the nucleotide sequence of SEQ ID NO:9 from nucleotide 118 to nucleotide 468; the nucleotide sequence of the full-length protein coding sequence of clone vf2\_1 deposited with the ATCC under accession number 98846; or the nucleotide sequence of a mature protein coding sequence of clone vf2\_1 deposited with

the ATCC under accession number 98846. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vf2\_1 deposited with the ATCC under accession number 98846. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:10, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity, the fragment comprising the amino acid sequence from amino acid 69 to amino acid 78 of SEQ ID NO:10.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:9.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

15

20

25

30

10

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:9, but excluding the poly(A) tail at the 3' end of SEQ ID NO:9; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vf2\_1 deposited with the ATCC under accession number 98846;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:9, but excluding the poly(A) tail at the 3' end of SEQ ID NO:9; and

(bb) the nucleotide sequence of the cDNA insert of clone vf2\_1 deposited with the ATCC under accession number 98846;

- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and

5

10

15

20

25

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:9, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:9 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:9, but excluding the poly(A) tail at the 3' end of SEQ ID NO:9. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:9 from nucleotide 22 to nucleotide 468, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:9 from nucleotide 22 to nucleotide 468, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:9 from nucleotide 22 to nucleotide 468. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:9 from nucleotide 118 to nucleotide 468, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:9 from nucleotide 118 to nucleotide 468, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:9 from nucleotide 118 to nucleotide 468.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:10;
- (b) a fragment of the amino acid sequence of SEQ ID NO:10, the fragment comprising eight contiguous amino acids of SEQ ID NO:10; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vf2\_1
   30 deposited with the ATCC under accession number 98846;
   the protein being substantially free from other mammalian proteins. Preferably such

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:10. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity, the fragment preferably

comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:10, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity, the fragment comprising the amino acid sequence from amino acid 69 to amino acid 78 of SEQ ID NO:10.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

5

10

15

20

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11 from nucleotide 124 to nucleotide 1641;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11 from nucleotide 262 to nucleotide 1641;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vg2\_1 deposited with the ATCC under accession number 98846;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vg2\_1 deposited with the ATCC under accession number 98846;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vg2\_1 deposited with the ATCC under accession number 98846;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vg2\_1 deposited with the ATCC under accession number 98846;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:12;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:12;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:11.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:11 from nucleotide 124 to nucleotide 1641; the nucleotide sequence of SEQ ID NO:11 from nucleotide 262 to nucleotide 1641; the nucleotide sequence of the full-length protein coding sequence of clone vg2\_1 deposited with the ATCC under accession number 98846; or the nucleotide sequence of a mature protein coding sequence of clone vg2\_1 deposited with the ATCC under accession number 98846. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vg2\_1 deposited with the ATCC under accession number 98846. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:12, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity, the fragment comprising the amino acid sequence from amino acid 248 to amino acid 257 of SEQ ID NO:12.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 20 ID NO:11.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:11, but excluding the poly(A) tail at the 3' end of SEQ ID NO:11; and
  - (ab) the nucleotide sequence of the cDNA insert of clonevg2\_1 deposited with the ATCC under accession number 98846;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

10

15

25

and

5

10

15

20

25

30

(b) a process comprising the steps of:

- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:11, but excluding the poly(A) tail at the 3' end of SEQ ID NO:11; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vg2\_1 deposited with the ATCC under accession number 98846;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:11, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:11 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:11, but excluding the poly(A) tail at the 3' end of SEQ ID NO:11. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:11 from nucleotide 124 to nucleotide 1641, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:11 from nucleotide 124 to nucleotide 1641, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:11 from nucleotide 124 to nucleotide 1641. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:11 from nucleotide 262 to nucleotide 1641, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:11 from nucleotide 262 to nucleotide 1641, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:11 from nucleotide 262 to nucleotide 1641.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:12;

(b) a fragment of the amino acid sequence of SEQ ID NO:12, the fragment comprising eight contiguous amino acids of SEQ ID NO:12; and

- (c) the amino acid sequence encoded by the cDNA insert of clone vg2\_1 deposited with the ATCC under accession number 98846;
- 5 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:12. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:12, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity, the fragment comprising the amino acid sequence from amino acid 248 to amino acid 257 of SEQ ID NO:12.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:13;

20

25

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:13 from nucleotide 380 to nucleotide 892;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:13 from nucleotide 416 to nucleotide 892:
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vj1\_1 deposited with the ATCC under accession number 98846;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vj1\_1 deposited with the ATCC under accession number 98846;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vj1\_1 deposited with the ATCC under accession number 98846;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vj1\_1 deposited with the ATCC under accession number 98846;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:14;

5

10

15

25

30

 (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:14;

- (j) a polynucleotide which is an allelic variant of a polynucleotide of(a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:13.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:13 from nucleotide 380 to nucleotide 892; the nucleotide sequence of SEQ ID NO:13 from nucleotide 416 to nucleotide 892; the nucleotide sequence of the full-length protein coding sequence of clone vj1\_1 deposited with the ATCC under accession number 98846; or the nucleotide sequence of a mature protein coding sequence of clone vj1\_1 deposited with the ATCC under accession number 98846. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vj1\_1 deposited with the ATCC under accession number 98846. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:14, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment comprising the amino acid sequence from amino acid 80 to amino acid 89 of SEQ ID NO:14.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:13.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

- (aa) SEQ ID NO:13; and
- (ab) the nucleotide sequence of the cDNA insert of clone vj1\_1 deposited with the ATCC under accession number 98846;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

5

10

15

20

25

30

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:13; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vj1\_1 deposited with the ATCC under accession number 98846;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:13, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:13 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:13. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:13 from nucleotide 380 to nucleotide 892, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:13 from nucleotide 380 to nucleotide 892, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:13 from nucleotide 380 to nucleotide 892. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:13 from nucleotide 892, and

extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:13 from nucleotide 416 to nucleotide 892, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:13 from nucleotide 416 to nucleotide 892.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:14;

5

10

15

20

25

30

- (b) a fragment of the amino acid sequence of SEQ ID NO:14, the fragment comprising eight contiguous amino acids of SEQ ID NO:14; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vj1\_1 deposited with the ATCC under accession number 98846;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:14. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:14, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment comprising the amino acid sequence from amino acid 80 to amino acid 89 of SEQ ID NO:14.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:15;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:15 from nucleotide 62 to nucleotide 1057;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:15 from nucleotide 659 to nucleotide 1057;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vl1\_1 deposited with the ATCC under accession number 98846;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vl1\_1 deposited with the ATCC under accession number 98846;

5

10

15

20

25

30

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vl1\_1 deposited with the ATCC under accession number 98846;

- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vl1\_1 deposited with the ATCC under accession number 98846;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:16;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:16 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:16;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:15.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:15 from nucleotide 62 to nucleotide 1057; the nucleotide sequence of SEQ ID NO:15 from nucleotide 659 to nucleotide 1057; the nucleotide sequence of the full-length protein coding sequence of clone vl1\_1 deposited with the ATCC under accession number 98846; or the nucleotide sequence of a mature protein coding sequence of clone vl1\_1 deposited with the ATCC under accession number 98846. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vl1\_1 deposited with the ATCC under accession number 98846. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:16 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:16, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:16 having biological activity, the fragment comprising the amino acid sequence from amino acid 161 to amino acid 170 of SEQ ID NO:16.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:15.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:15, but excluding the poly(A) tail at the 3' end of SEQ ID NO:15; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vl1\_1 deposited with the ATCC under accession number 98846;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

5

10

15

20

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:15, but excluding the poly(A) tail at the 3' end of SEQ ID NO:15; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vl1\_1 deposited with the ATCC under accession number 98846;
  - (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
    - (iii) amplifying human DNA sequences; and
    - (iv) isolating the polynucleotide products of step (b)(iii).
- Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:15, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:15 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:15, but excluding the poly(A) tail at the 3' end of SEQ ID NO:15. Also preferably the

polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:15 from nucleotide 62 to nucleotide 1057, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:15 from nucleotide 62 to nucleotide 1057, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:15 from nucleotide 62 to nucleotide 1057. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:15 from nucleotide 659 to nucleotide 1057, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:15 from nucleotide 659 to nucleotide 1057, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:15 from nucleotide 659 to nucleotide 1057.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

15

10

- (a) the amino acid sequence of SEQ ID NO:16;
- (b) a fragment of the amino acid sequence of SEQ ID NO:16, the fragment comprising eight contiguous amino acids of SEQ ID NO:16; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vl1\_1 deposited with the ATCC under accession number 98846;
- 20 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:16. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:16 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:16, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:16 having biological activity, the fragment comprising the amino acid sequence from amino acid 161 to amino acid 170 of SEQ ID NO:16.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ IDNO:17;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:17 from nucleotide 74 to nucleotide 529;

5

10

15

20

25

30

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:17 from nucleotide 140 to nucleotide 529;

- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vk2\_1 deposited with the ATCC under accession number 98838;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vk2\_1 deposited with the ATCC under accession number 98838:
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vk2\_1 deposited with the ATCC under accession number 98838;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vk2\_1 deposited with the ATCC under accession number 98838;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:18;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:18 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:18;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of(a)-(g) above;
  - (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:17.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:17 from nucleotide 74 to nucleotide 529; the nucleotide sequence of SEQ ID NO:17 from nucleotide 140 to nucleotide 529; the nucleotide sequence of the full-length protein coding sequence of clone vk2\_1 deposited with the ATCC under accession number 98838; or the nucleotide sequence of a mature protein coding sequence of clone vk2\_1 deposited with the ATCC under accession number 98838. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert

of clone vk2\_1 deposited with the ATCC under accession number 98838. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:18 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:18, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:18 having biological activity, the fragment comprising the amino acid sequence from amino acid 71 to amino acid 80 of SEQ ID NO:18.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 10 ID NO:17.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:17, but excluding the poly(A) tail at the 3' end of SEQ ID NO:17; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vk2\_1 deposited with the ATCC under accession number 98838;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);
- 25 and
- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:17, but excluding the poly(A) tail at the 3' end of SEQ ID NO:17; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vk2\_1 deposited with the ATCC under accession number 98838;

15

PCT/US99/19351 WO 00/11015

> (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

- (iii) amplifying human DNA sequences; and
- (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:17, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:17 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:17, but excluding the poly(A) tail at the 3' end of SEQ ID NO:17. Also preferably the 10 polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:17 from nucleotide 74 to nucleotide 529, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:17 from nucleotide 74 to nucleotide 529, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:17 from nucleotide 15 74 to nucleotide 529. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:17 from nucleotide 140 to nucleotide 529, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:17 from nucleotide 140 to nucleotide 529, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:17 from nucleotide 140 to nucleotide 529.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

> (a) the amino acid sequence of SEQ ID NO:18;

20

30

- 25 a fragment of the amino acid sequence of SEQ ID NO:18, the (b) fragment comprising eight contiguous amino acids of SEQ ID NO:18; and
  - (c) the amino acid sequence encoded by the cDNA insert of clone vk2\_1 deposited with the ATCC under accession number 98838;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:18. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:18 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:18, or a protein comprising a fragment of the amino acid sequence of SEQ

ID NO:18 having biological activity, the fragment comprising the amino acid sequence from amino acid 71 to amino acid 80 of SEQ ID NO:18.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

5

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19 from nucleotide 174 to nucleotide 3170;

10

- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19 from nucleotide 1098 to nucleotide 3170;
- (d) a polynucleotide comprising the nucleotide sequence of the fulllength protein coding sequence of clone vb21\_1 deposited with the ATCC under accession number 98862;

15

- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vb21\_1 deposited with the ATCC under accession number 98862;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vb21\_1 deposited with the ATCC under accession number 98862;

20

- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vb21\_1 deposited with the ATCC under accession number 98862;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:20;

25

- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:20;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of(a)-(g) above;

- a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:19.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:19 from nucleotide 174 to nucleotide 3170; the nucleotide sequence of SEQ ID NO:19 from nucleotide 1098 to nucleotide 3170; the nucleotide sequence of the full-length protein coding sequence of clone vb21\_1 deposited with the ATCC under accession number 98862; or the nucleotide sequence of a mature protein coding sequence of clone vb21\_1 deposited with the ATCC under accession number 98862. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vb21\_1 deposited with the ATCC under accession number 98862. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:20, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20 having biological activity, the fragment comprising the amino acid sequence from amino acid 494 to amino acid 503 of SEQ ID NO:20.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:19.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:19, but excluding the poly(A) tail at the 3' end of SEQ ID NO:19; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vb21\_1 deposited with the ATCC under accession number 98862;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

10

15

20

and

5

10

15

20

25

30

(b) a process comprising the steps of:

- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:19, but excluding the poly(A) tail at the 3' end of SEQ ID NO:19; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vb21\_1 deposited with the ATCC under accession number 98862;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:19, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:19 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:19, but excluding the poly(A) tail at the 3' end of SEQ ID NO:19. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:19 from nucleotide 174 to nucleotide 3170, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:19 from nucleotide 174 to nucleotide 3170, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:19 from nucleotide 174 to nucleotide 3170. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:19 from nucleotide 1098 to nucleotide 3170, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:19 from nucleotide 1098 to nucleotide 3170, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:19 from nucleotide 1098 to nucleotide 3170.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:20;

(b) a fragment of the amino acid sequence of SEQ ID NO:20, the fragment comprising eight contiguous amino acids of SEQ ID NO:20; and

- (c) the amino acid sequence encoded by the cDNA insert of clone vb21\_1 deposited with the ATCC under accession number 98862;
- 5 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:20. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:20, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20 having biological activity, the fragment comprising the amino acid sequence from amino acid 494 to amino acid 503 of SEQ ID NO:20.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:21;

20

25

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:21 from nucleotide 74 to nucleotide 1453;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:21 from nucleotide 224 to nucleotide 1453;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc35\_1 deposited with the ATCC under accession number 98862;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc35\_1 deposited with the ATCC under accession number 98862:
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc35\_1 deposited with the ATCC under accession number 98862;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc35\_1 deposited with the ATCC under accession number 98862;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:22;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:22;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;

5

10

15

20

25

30

- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:21.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:21 from nucleotide 74 to nucleotide 1453; the nucleotide sequence of SEQ ID NO:21 from nucleotide 224 to nucleotide 1453; the nucleotide sequence of the full-length protein coding sequence of clone vc35\_1 deposited with the ATCC under accession number 98862; or the nucleotide sequence of a mature protein coding sequence of clone vc35\_1 deposited with the ATCC under accession number 98862. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc35\_1 deposited with the ATCC under accession number 98862. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:22, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22 having biological activity, the fragment comprising the amino acid sequence from amino acid 225 to amino acid 234 of SEQ ID NO:22.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:21.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of: SEQ ID NO:21, but excluding the poly(A) tail at the (aa) 5 3' end of SEQ ID NO:21; and (ab) the nucleotide sequence of the cDNA insert of clone vc35\_1 deposited with the ATCC under accession number 98862; hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and 10 (iii) isolating the DNA polynucleotides detected with the probe(s); and (b) a process comprising the steps of: preparing one or more polynucleotide primers that 15 hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of: SEQ ID NO:21, but excluding the poly(A) tail at the (ba) 3' end of SEQ ID NO:21; and the nucleotide sequence of the cDNA insert of clone 20 vc35\_1 deposited with the ATCC under accession number 98862; hybridizing said primer(s) to human genomic DNA in (ii) conditions at least as stringent as 4X SSC at 50 degrees C; amplifying human DNA sequences; and (iii) (iv) isolating the polynucleotide products of step (b)(iii). 25 Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:21, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:21 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:21, but excluding the poly(A) tail at the 3' end of SEQ ID NO:21. Also preferably the 30 polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:21 from nucleotide 74 to nucleotide 1453, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:21 from nucleotide 74 to nucleotide 1453, to a nucleotide

sequence corresponding to the 3' end of said sequence of SEQ ID NO:21 from nucleotide

74 to nucleotide 1453. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:21 from nucleotide 224 to nucleotide 1453, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:21 from nucleotide 224 to nucleotide 1453, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:21 from nucleotide 224 to nucleotide 1453.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10

5

- (a) the amino acid sequence of SEQ ID NO:22;
- (b) a fragment of the amino acid sequence of SEQ ID NO:22, the fragment comprising eight contiguous amino acids of SEQ ID NO:22; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc35\_1 deposited with the ATCC under accession number 98862;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:22. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:22, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22 having biological activity, the fragment comprising the amino acid sequence from amino acid 225 to amino acid 234 of SEQ ID NO:22.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:23:
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:23 from nucleotide 135 to nucleotide 368;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:23 from nucleotide 243 to nucleotide 368;
- (d) a polynucleotide comprising the nucleotide sequence of the fulllength protein coding sequence of clone vc36\_1 deposited with the ATCC under accession number 98862;

5

10

15

20

25

30

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc36\_1 deposited with the ATCC under accession number 98862;

- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc36\_1 deposited with the ATCC under accession number 98862;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc36\_1 deposited with the ATCC under accession number 98862;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:24;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:24;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:23.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:23 from nucleotide 135 to nucleotide 368; the nucleotide sequence of SEQ ID NO:23 from nucleotide 243 to nucleotide 368; the nucleotide sequence of the full-length protein coding sequence of clone vc36\_1 deposited with the ATCC under accession number 98862; or the nucleotide sequence of a mature protein coding sequence of clone vc36\_1 deposited with the ATCC under accession number 98862. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc36\_1 deposited with the ATCC under accession number 98862. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:24, or a polynucleotide

encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity, the fragment comprising the amino acid sequence from amino acid 34 to amino acid 43 of SEQ ID NO:24.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 5 ID NO:23.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:23, but excluding the poly(A) tail at the 3' end of SEQ ID NO:23; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vc36\_1 deposited with the ATCC under accession number 98862;
  - (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
  - (iii) isolating the DNA polynucleotides detected with the probe(s);
- 20 and

10

15

25

30

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:23, but excluding the poly(A) tail at the 3' end of SEQ ID NO:23; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vc36\_1 deposited with the ATCC under accession number 98862;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:23, and

extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:23 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:23, but excluding the poly(A) tail at the 3' end of SEQ ID NO:23. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:23 from nucleotide 135 to nucleotide 368, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:23 from nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:23 from nucleotide 135 to nucleotide 368. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:23 from nucleotide 243 to nucleotide 368, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:23 from nucleotide 243 to nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:23 from nucleotide 243 to nucleotide 368, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:23 from nucleotide 243 to nucleotide 368, to a nucleotide 243 to nucleotide 368.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:24;

15

20

25

30

- (b) a fragment of the amino acid sequence of SEQ ID NO:24, the fragment comprising eight contiguous amino acids of SEQ ID NO:24; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc36\_1 deposited with the ATCC under accession number 98862;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:24. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:24, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity, the fragment comprising the amino acid sequence from amino acid 34 to amino acid 43 of SEQ ID NO:24.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:25;

PCT/US99/19351

WO 00/11015

5

10

15

20

25

30

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:25 from nucleotide 370 to nucleotide 1662;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc38\_1 deposited with the ATCC under accession number 98862;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc38\_1 deposited with the ATCC under accession number 98862;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc38\_1 deposited with the ATCC under accession number 98862;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc38\_1 deposited with the ATCC under accession number 98862;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:26;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:26;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above;
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above;
- (k) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h); and
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h) and that has a length that is at least 25% of the length of SEQ ID NO:25.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:25 from nucleotide 370 to nucleotide 1662; the nucleotide sequence of the full-length protein coding sequence of clone vc38\_1 deposited with the ATCC under accession number 98862; or the nucleotide sequence of a mature protein coding sequence of clone vc38\_1 deposited with the ATCC under accession number 98862. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc38\_1 deposited with the ATCC under accession number 98862.

In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:26, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26 having biological activity, the fragment comprising the amino acid sequence from amino acid 210 to amino acid 219 of SEQ ID NO:26.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:25.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:25, but excluding the poly(A) tail at the 3' end of SEQ ID NO:25; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vc38\_1 deposited with the ATCC under accession number 98862;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:25, but excluding the poly(A) tail at the 3' end of SEQ ID NO:25; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vc38\_1 deposited with the ATCC under accession number 98862;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;

30

25

10

15

- (iii) amplifying human DNA sequences; and
- (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:25, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:25 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:25, but excluding the poly(A) tail at the 3' end of SEQ ID NO:25. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:25 from nucleotide 370 to nucleotide 1662, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:25 from nucleotide 1662, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:25 from nucleotide 370 to nucleotide 1662.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:26;

10

15

20

25

- (b) a fragment of the amino acid sequence of SEQ ID NO:26, the fragment comprising eight contiguous amino acids of SEQ ID NO:26; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc38\_1 deposited with the ATCC under accession number 98862;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:26. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:26, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26 having biological activity, the fragment comprising the amino acid sequence from amino acid 210 to amino acid 219 of SEQ ID NO:26.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:27;

5

10

15

20

25

30

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:27 from nucleotide 105 to nucleotide 365;

- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:27 from nucleotide 147 to nucleotide 365;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc39\_1 deposited with the ATCC under accession number 98862;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc39\_1 deposited with the ATCC under accession number 98862;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc39\_1 deposited with the ATCC under accession number 98862;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc39\_1 deposited with the ATCC under accession number 98862;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:28;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:28;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of(a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:27.
- Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:27 from nucleotide 105 to nucleotide 365; the nucleotide sequence of SEQ ID NO:27 from nucleotide 147 to nucleotide 365; the nucleotide sequence of the full-length protein coding sequence of clone vc39\_1 deposited with the ATCC under accession number 98862; or the nucleotide sequence of a mature protein coding sequence of clone vc39\_1 deposited

with the ATCC under accession number 98862. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc39\_1 deposited with the ATCC under accession number 98862. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:28, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment comprising the amino acid sequence from amino acid 38 to amino acid 47 of SEQ ID NO:28.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:27.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

15

20

25

30

10

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:27, but excluding the poly(A) tail at the 3' end of SEQ ID NO:27; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vc39\_1 deposited with the ATCC under accession number 98862;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:27, but excluding the poly(A) tail at the 3' end of SEQ ID NO:27; and

(bb) the nucleotide sequence of the cDNA insert of clone vc39\_1 deposited with the ATCC under accession number 98862;

- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and

5

10

15

20

25

30

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:27, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:27 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:27, but excluding the poly(A) tail at the 3' end of SEQ ID NO:27. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:27 from nucleotide 105 to nucleotide 365, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:27 from nucleotide 105 to nucleotide 365, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:27 from nucleotide 105 to nucleotide 365. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:27 from nucleotide 147 to nucleotide 365, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:27 from nucleotide 147 to nucleotide 365, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:27 from nucleotide 147 to nucleotide 365.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:28;
- (b) a fragment of the amino acid sequence of SEQ ID NO:28, the fragment comprising eight contiguous amino acids of SEQ ID NO:28; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc39\_1 deposited with the ATCC under accession number 98862;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:28. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment preferably

comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:28, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment comprising the amino acid sequence from amino acid 38 to amino acid 47 of SEQ ID NO:28.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

5

10

15

20

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:29;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:29 from nucleotide 35 to nucleotide 1066;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:29 from nucleotide 128 to nucleotide 1066;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc40\_1 deposited with the ATCC under accession number 98862;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc40\_1 deposited with the ATCC under accession number 98862;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc40\_1 deposited with the ATCC under accession number 98862;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc40\_1 deposited with the ATCC under accession number 98862;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:30;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:30;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:29.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:29 from nucleotide 35 to nucleotide 1066; the nucleotide sequence of SEQ ID NO:29 from nucleotide 128 to nucleotide 1066; the nucleotide sequence of the full-length protein coding sequence of clone vc40\_1 deposited with the ATCC under accession number 98862; or the nucleotide sequence of a mature protein coding sequence of clone vc40\_1 deposited with the ATCC under accession number 98862. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc40\_1 deposited with the ATCC under accession number 98862. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:30, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30 having biological activity, the fragment comprising the amino acid sequence from amino acid 176 of SEQ ID NO:30.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:29.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:29, but excluding the poly(A) tail at the 3' end of SEQ ID NO:29; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vc40\_1 deposited with the ATCC under accession number 98862;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

30

5

10

15

20

and

5

10

15

20

25

30

(b) a process comprising the steps of:

- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:29, but excluding the poly(A) tail at the 3' end of SEQ ID NO:29; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vc40\_1 deposited with the ATCC under accession number 98862;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:29, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:29 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:29, but excluding the poly(A) tail at the 3' end of SEQ ID NO:29. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:29 from nucleotide 35 to nucleotide 1066, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:29 from nucleotide 35 to nucleotide 1066, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:29 from nucleotide 35 to nucleotide 1066. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEO ID NO:29 from nucleotide 128 to nucleotide 1066, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:29 from nucleotide 128 to nucleotide 1066, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:29 from nucleotide 128 to nucleotide 1066.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:30;

(b) a fragment of the amino acid sequence of SEQ ID NO:30, the fragment comprising eight contiguous amino acids of SEQ ID NO:30; and

- (c) the amino acid sequence encoded by the cDNA insert of clone vc40\_1 deposited with the ATCC under accession number 98862;
- 5 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:30. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:30, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30 having biological activity, the fragment comprising the amino acid sequence from amino acid 167 to amino acid 176 of SEQ ID NO:30.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:31;

20

25

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:31 from nucleotide 38 to nucleotide 553;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:31 from nucleotide 104 to nucleotide 553;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc46\_1 deposited with the ATCC under accession number 98862;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc46\_1 deposited with the ATCC under accession number 98862;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc46\_1 deposited with the ATCC under accession number 98862;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc46\_1 deposited with the ATCC under accession number 98862;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:32;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:32 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:32;

- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- $\begin{tabular}{ll} (k) & a polynucleotide which encodes a species homologue of the protein of (h) or (i) above; \end{tabular}$
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:31.

5

15

20

25

30

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:31 from nucleotide 38 to nucleotide 553; the nucleotide sequence of SEQ ID NO:31 from nucleotide 104 to nucleotide 553; the nucleotide sequence of the full-length protein coding sequence of clone vc46\_1 deposited with the ATCC under accession number 98862; or the nucleotide sequence of a mature protein coding sequence of clone vc46\_1 deposited with the ATCC under accession number 98862. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc46\_1 deposited with the ATCC under accession number 98862. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:32 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:32, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:32 having biological activity, the fragment comprising the amino acid sequence from amino acid 81 to amino acid 90 of SEQ ID NO:32.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:31.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

	(i) preparing one or more polynucleotide probes that hybridize
	in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group
	consisting of:
	(aa) SEQ ID NO:31, but excluding the poly(A) tail at the
5	3' end of SEQ ID NO:31; and
	(ab) the nucleotide sequence of the cDNA insert of clone
	vc46_1 deposited with the ATCC under accession number 98862;
	(ii) hybridizing said probe(s) to human genomic DNA in
	conditions at least as stringent as 4X SSC at 50 degrees C; and
10	(iii) isolating the DNA polynucleotides detected with the
	probe(s);
	and
	(b) a process comprising the steps of:
	(i) preparing one or more polynucleotide primers that
15	hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from
	the group consisting of:
	(ba) SEQ ID NO:31, but excluding the poly(A) tail at the
	3' end of SEQ ID NO:31; and
	(bb) the nucleotide sequence of the cDNA insert of clone
20	vc46_1 deposited with the ATCC under accession number 98862;
	(ii) hybridizing said primer(s) to human genomic DNA in
	conditions at least as stringent as 4X SSC at 50 degrees C;
	(iii) amplifying human DNA sequences; and
	(iv) isolating the polynucleotide products of step (b)(iii).
25	Preferably the polynucleotide isolated according to the above process comprises a
	nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:31, and
	extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ
	ID NO:31 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:31, but
	excluding the poly(A) tail at the 3' end of SEQ ID NO:31. Also preferably the
30	polynucleotide isolated according to the above process comprises a nucleotide sequence
	corresponding to the cDNA sequence of SEQ ID NO:31 from nucleotide 38 to nucleotide
	553, and extending contiguously from a nucleotide sequence corresponding to the 5' and

of said sequence of SEQ ID NO:31 from nucleotide 38 to nucleotide 553, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:31 from nucleotide

38 to nucleotide 553. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:31 from nucleotide 104 to nucleotide 553, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:31 from nucleotide 104 to nucleotide 553, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:31 from nucleotide 104 to nucleotide 553.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10

- (a) the amino acid sequence of SEQ ID NO:32;
- (b) a fragment of the amino acid sequence of SEQ ID NO:32, the fragment comprising eight contiguous amino acids of SEQ ID NO:32; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc46\_1 deposited with the ATCC under accession number 98862;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:32. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:32 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:32, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:32 having biological activity, the fragment comprising the amino acid sequence from amino acid 81 to amino acid 90 of SEQ ID NO:32.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:33;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:33 from nucleotide 164 to nucleotide 2548;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:33 from nucleotide 242 to nucleotide 2548;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc49\_1 deposited with the ATCC under accession number 98862;

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc49\_1 deposited with the ATCC under accession number 98862;

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc49\_1 deposited with the ATCC under accession number 98862;

5

10

15

20

25

30

- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc49\_1 deposited with the ATCC under accession number 98862;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:34;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:34;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein
   of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:33.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:33 from nucleotide 164 to nucleotide 2548; the nucleotide sequence of SEQ ID NO:33 from nucleotide 242 to nucleotide 2548; the nucleotide sequence of the full-length protein coding sequence of clone vc49\_1 deposited with the ATCC under accession number 98862; or the nucleotide sequence of a mature protein coding sequence of clone vc49\_1 deposited with the ATCC under accession number 98862. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc49\_1 deposited with the ATCC under accession number 98862. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:34, or a polynucleotide

encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the fragment comprising the amino acid sequence from amino acid 392 to amino acid 401 of SEQ ID NO:34.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 5 ID NO:33.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:33, but excluding the poly(A) tail at the 3' end of SEQ ID NO:33; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vc49\_1 deposited with the ATCC under accession number 98862;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);
- 20 and

10

15

25

30

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:33, but excluding the poly(A) tail at the 3' end of SEQ ID NO:33; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vc49\_1 deposited with the ATCC under accession number 98862;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEO ID NO:33, and

extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:33 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:33, but excluding the poly(A) tail at the 3' end of SEQ ID NO:33. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:33 from nucleotide 164 to nucleotide 2548, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:33 from nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:33 from nucleotide 164 to nucleotide 2548. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:33 from nucleotide 242 to nucleotide 2548, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:33 from nucleotide 242 to nucleotide 2548, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:33 from nucleotide 2548.

5

10

15

20

25

30

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:34;
- (b) a fragment of the amino acid sequence of SEQ ID NO:34, the fragment comprising eight contiguous amino acids of SEQ ID NO:34; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc49\_1 deposited with the ATCC under accession number 98862;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:34. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:34, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the fragment comprising the amino acid sequence from amino acid 392 to amino acid 401 of SEQ ID NO:34.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:35;

5

10

15

20

25

(b). a polynucleotide comprising the nucleotide sequence of SEQ ID NO:35 from nucleotide 150 to nucleotide 776;

- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:35 from nucleotide 246 to nucleotide 776;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc50\_1 deposited with the ATCC under accession number 98862;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc50\_1 deposited with the ATCC under accession number 98862;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc50\_1 deposited with the ATCC under accession number 98862;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc50\_1 deposited with the ATCC under accession number 98862;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:36;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:36;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- a polynucleotide which encodes a species homologue of the protein
   of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:35.
- Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:35 from nucleotide 150 to nucleotide 776; the nucleotide sequence of SEQ ID NO:35 from nucleotide 246 to nucleotide 776; the nucleotide sequence of the full-length protein coding sequence of clone vc50\_1 deposited with the ATCC under accession number 98862; or the nucleotide sequence of a mature protein coding sequence of clone vc50\_1 deposited

with the ATCC under accession number 98862. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc50\_1 deposited with the ATCC under accession number 98862. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:36, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36 having biological activity, the fragment comprising the amino acid sequence from amino acid 99 to amino acid 108 of SEQ ID NO:36.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:35.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

15

20

25

30

10

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:35, but excluding the poly(A) tail at the 3' end of SEQ ID NO:35; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vc50\_1 deposited with the ATCC under accession number 98862;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:35, but excluding the poly(A) tail at the 3' end of SEQ ID NO:35; and

(bb) the nucleotide sequence of the cDNA insert of clone vc50\_1 deposited with the ATCC under accession number 98862;

- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and

5

10

15

20

25

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:35, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEO ID NO:35 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:35, but excluding the poly(A) tail at the 3' end of SEQ ID NO:35. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:35 from nucleotide 150 to nucleotide 776, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:35 from nucleotide 150 to nucleotide 776, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:35 from nucleotide 150 to nucleotide 776. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:35 from nucleotide 246 to nucleotide 776, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:35 from nucleotide 246 to nucleotide 776, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:35 from nucleotide 246 to nucleotide 776.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:36;
- (b) a fragment of the amino acid sequence of SEQ ID NO:36, the fragment comprising eight contiguous amino acids of SEQ ID NO:36; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc50\_1 deposited with the ATCC under accession number 98862; the protein being substantially free from other mammalian proteins. Preferably such

protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:36. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36 having biological activity, the fragment preferably

comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:36, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36 having biological activity, the fragment comprising the amino acid sequence from amino acid 99 to amino acid 108 of SEO ID NO:36.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

5

10

15

20

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:37;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:37 from nucleotide 139 to nucleotide 1308;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:37 from nucleotide 211 to nucleotide 1308;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc51\_1 deposited with the ATCC under accession number 98862;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc51\_1 deposited with the ATCC under accession number 98862;
  - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc51\_1 deposited with the ATCC under accession number 98862;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc51\_1 deposited with the ATCC under accession number 98862;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:38;
  - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:38 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:38;
  - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
  - $\begin{tabular}{ll} (k) & a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ; \end{tabular}$
  - (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:37.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:37 from nucleotide 139 to nucleotide 1308; the nucleotide sequence of SEQ ID NO:37 from nucleotide 211 to nucleotide 1308; the nucleotide sequence of the full-length protein coding sequence of clone vc51\_1 deposited with the ATCC under accession number 98862; or the nucleotide sequence of a mature protein coding sequence of clone vc51\_1 deposited with the ATCC under accession number 98862. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc51\_1 deposited with the ATCC under accession number 98862. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:38 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:38, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:38 having biological activity, the fragment comprising the amino acid sequence from amino acid 190 to amino acid 199 of SEQ ID NO:38.

10

15

25

30

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 20 ID NO:37.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:37, but excluding the poly(A) tail at the 3' end of SEQ ID NO:37; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vc51\_1 deposited with the ATCC under accession number 98862;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

5

10

15

20

25

30

(b) a process comprising the steps of:

- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:37, but excluding the poly(A) tail at the 3' end of SEQ ID NO:37; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vc51\_1 deposited with the ATCC under accession number 98862;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:37, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:37 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:37, but excluding the poly(A) tail at the 3' end of SEQ ID NO:37. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:37 from nucleotide 139 to nucleotide 1308, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:37 from nucleotide 139 to nucleotide 1308, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:37 from nucleotide 139 to nucleotide 1308. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:37 from nucleotide 211 to nucleotide 1308, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:37 from nucleotide 211 to nucleotide 1308, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:37 from nucleotide 211 to nucleotide 1308.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:38;

(b) a fragment of the amino acid sequence of SEQ ID NO:38, the fragment comprising eight contiguous amino acids of SEQ ID NO:38; and

- (c) the amino acid sequence encoded by the cDNA insert of clone vc51\_1 deposited with the ATCC under accession number 98862;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:38. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:38 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:38, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:38 having biological activity, the fragment comprising the amino acid sequence from amino acid 190 to amino acid 199 of SEQ ID NO:38.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:39;

20

25

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:39 from nucleotide 21 to nucleotide 1142;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:39 from nucleotide 114 to nucleotide 1142;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc52\_1 deposited with the ATCC under accession number 98862;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc52\_1 deposited with the ATCC under accession number 98862;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc52\_1 deposited with the ATCC under accession number 98862;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc52\_1 deposited with the ATCC under accession number 98862;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:40;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:40;

- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:39.

5

15

20

25

30

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:39 from nucleotide 21 to nucleotide 1142; the nucleotide sequence of SEQ ID NO:39 from nucleotide 114 to nucleotide 1142; the nucleotide sequence of the full-length protein coding sequence of clone vc52\_1 deposited with the ATCC under accession number 98862; or the nucleotide sequence of a mature protein coding sequence of clone vc52\_1 deposited with the ATCC under accession number 98862. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc52\_1 deposited with the ATCC under accession number 98862. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:40, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40 having biological activity, the fragment comprising the amino acid sequence from amino acid 182 to amino acid 191 of SEQ ID NO:40.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:39.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

PCT/US99/19351 WO 00/11015

	(i) preparing one or more polynucleotide probes that hybridiz
	in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group
	consisting of:
	(aa) SEQ ID NO:39, but excluding the poly(A) tail at the
5	3' end of SEQ ID NO:39; and
	(ab) the nucleotide sequence of the cDNA insert of clone
	vc52_1 deposited with the ATCC under accession number 98862
	(ii) hybridizing said probe(s) to human genomic DNA in
	conditions at least as stringent as 4X SSC at 50 degrees C; and
10	(iii) isolating the DNA polynucleotides detected with the
	probe(s);
	and
	(b) a process comprising the steps of:
	(i) preparing one or more polynucleotide primers tha
15	hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from
	the group consisting of:
	(ba) SEQ ID NO:39, but excluding the poly(A) tail at the
	3' end of SEQ ID NO:39; and
	(bb) the nucleotide sequence of the cDNA insert of clone
20	vc52_1 deposited with the ATCC under accession number 98862
	(ii) hybridizing said primer(s) to human genomic DNA ir
	conditions at least as stringent as 4X SSC at 50 degrees C;
	(iii) amplifying human DNA sequences; and
	(iv) isolating the polynucleotide products of step (b)(iii).
25	Preferably the polynucleotide isolated according to the above process comprises a
	nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:39, and
	extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ
	ID NO:39 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:39, but
	excluding the poly(A) tail at the 3' end of SEQ ID NO:39. Also preferably the
30	polynucleotide isolated according to the above process comprises a nucleotide sequence
	corresponding to the cDNA sequence of SEQ ID NO:39 from nucleotide 21 to nucleotide
	1142, and extending contiguously from a nucleotide sequence corresponding to the 5' end
	of said sequence of SEQ ID NO:39 from nucleotide 21 to nucleotide 1142, to a nucleotide

sequence corresponding to the 3' end of said sequence of SEQ ID NO:39 from nucleotide

21 to nucleotide 1142. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ·ID NO:39 from nucleotide 114 to nucleotide 1142, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:39 from nucleotide 114 to nucleotide 1142, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:39 from nucleotide 114 to nucleotide 1142.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10

- (a) the amino acid sequence of SEQ ID NO:40;
- (b) a fragment of the amino acid sequence of SEQ ID NO:40, the fragment comprising eight contiguous amino acids of SEQ ID NO:40; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc52\_1 deposited with the ATCC under accession number 98862;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:40. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:40, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40 having biological activity, the fragment comprising the amino acid sequence from amino acid 182 to amino acid 191 of SEQ ID NO:40.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:41;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:41 from nucleotide 13 to nucleotide 1416;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:41 from nucleotide 346 to nucleotide 1416;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc33\_1 deposited with the ATCC under accession number 98886;

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc33\_1 deposited with the ATCC under accession number 98886;

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc33\_1 deposited with the ATCC under accession number 98886;

5

10

15

20

30

- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc33\_1 deposited with the ATCC under accession number 98886;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:42;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:42 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:42;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of(a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:41.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:41 from nucleotide 13 to nucleotide 1416; the nucleotide sequence of SEQ ID NO:41 from nucleotide 346 to nucleotide 1416; the nucleotide sequence of the full-length protein coding sequence of clone vc33\_1 deposited with the ATCC under accession number 98886; or the nucleotide sequence of a mature protein coding sequence of clone vc33\_1 deposited with the ATCC under accession number 98886. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc33\_1 deposited with the ATCC under accession number 98886. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:42 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:42, or a polynucleotide

encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:42 having biological activity, the fragment comprising the amino acid sequence from amino acid 229 to amino acid 238 of SEQ ID NO:42.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 5 ID NO:41.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:41, but excluding the poly(A) tail at the 3' end of SEQ ID NO:41; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vc33\_1 deposited with the ATCC under accession number 98886;
  - (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
  - (iii) isolating the DNA polynucleotides detected with the probe(s);
- 20 and

10

15

25

30

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:41, but excluding the poly(A) tail at the 3' end of SEQ ID NO:41; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vc33\_1 deposited with the ATCC under accession number 98886;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:41, and

extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:41 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:41, but excluding the poly(A) tail at the 3' end of SEQ ID NO:41. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:41 from nucleotide 13 to nucleotide 1416, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:41 from nucleotide 13 to nucleotide 1416, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:41 from nucleotide 13 to nucleotide 1416. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:41 from nucleotide 346 to nucleotide 1416, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:41 from nucleotide 346 to nucleotide 1416, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:41 from nucleotide 346 to nucleotide 1416, to a nucleotide 346 to nucleotide 1416.

10

15

20

25

30

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:42;
- (b) a fragment of the amino acid sequence of SEQ ID NO:42, the fragment comprising eight contiguous amino acids of SEQ ID NO:42; and
  - (c) the amino acid sequence encoded by the cDNA insert of clone vc33\_1 deposited with the ATCC under accession number 98886;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:42. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:42 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:42, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:42 having biological activity, the fragment comprising the amino acid sequence from amino acid 229 to amino acid 238 of SEQ ID NO:42.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:43;

5

10

15

20

25

30

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:43 from nucleotide 232 to nucleotide 1461;

- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:43 from nucleotide 280 to nucleotide 1461;
- (d) a polynucleotide comprising the nucleotide sequence of the fulllength protein coding sequence of clone vc34\_1 deposited with the ATCC under accession number 98886;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc34\_1 deposited with the ATCC under accession number 98886;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc34\_1 deposited with the ATCC under accession number 98886;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc34\_1 deposited with the ATCC under accession number 98886;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:44;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:44;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:43.
- Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:43 from nucleotide 232 to nucleotide 1461; the nucleotide sequence of SEQ ID NO:43 from nucleotide 280 to nucleotide 1461; the nucleotide sequence of the full-length protein coding sequence of clone vc34\_1 deposited with the ATCC under accession number 98886; or the nucleotide sequence of a mature protein coding sequence of clone vc34\_1 deposited

with the ATCC under accession number 98886. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc34\_1 deposited with the ATCC under accession number 98886. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:44, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44 having biological activity, the fragment comprising the amino acid sequence from amino acid 200 to amino acid 209 of SEQ ID NO:44.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:43.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

15

20

25

30

10

5

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:43, but excluding the poly(A) tail at the 3' end of SEQ ID NO:43; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vc34\_1 deposited with the ATCC under accession number 98886;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:43, but excluding the poly(A) tail at the 3' end of SEQ ID NO:43; and

(bb) the nucleotide sequence of the cDNA insert of clone vc34\_1 deposited with the ATCC under accession number 98886;

- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and

5

10

15

20

25

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:43, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:43 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:43, but excluding the poly(A) tail at the 3' end of SEQ ID NO:43. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:43 from nucleotide 232 to nucleotide 1461, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:43 from nucleotide 232 to nucleotide 1461, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:43 from nucleotide 232 to nucleotide 1461. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:43 from nucleotide 280 to nucleotide 1461, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:43 from nucleotide 280 to nucleotide 1461, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:43 from nucleotide 280 to nucleotide 1461.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:44;
- (b) a fragment of the amino acid sequence of SEQ ID NO:44, the fragment comprising eight contiguous amino acids of SEQ ID NO:44; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc34\_1 deposited with the ATCC under accession number 98886; the protein being substantially free from other mammalian proteins. Preferably such

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:44. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44 having biological activity, the fragment preferably

comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:44, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44 having biological activity, the fragment comprising the amino acid sequence from amino acid 200 to amino acid 209 of SEQ ID NO:44.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

5

10

15

20

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:45;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:45 from nucleotide 1922 to nucleotide 2350;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:45 from nucleotide 2237 to nucleotide 2350;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc47\_1 deposited with the ATCC under accession number 98886;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc47\_1 deposited with the ATCC under accession number 98886;
  - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc47\_1 deposited with the ATCC under accession number 98886;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc47\_1 deposited with the ATCC under accession number 98886;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:46;
  - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:46;
  - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
  - $\begin{tabular}{ll} (k) & a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ; \end{tabular}$
  - (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

PCT/US99/19351 WO 00/11015

> a polynucleotide that hybridizes under stringent conditions to any (m) one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:45.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID 5 NO:45 from nucleotide 1922 to nucleotide 2350; the nucleotide sequence of SEQ ID NO:45 from nucleotide 2237 to nucleotide 2350; the nucleotide sequence of the full-length protein coding sequence of clone vc47\_1 deposited with the ATCC under accession number 98886; or the nucleotide sequence of a mature protein coding sequence of clone vc47\_1 deposited with the ATCC under accession number 98886. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc47\_1 deposited with the ATCC under accession number 98886. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:46, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46 having biological activity, the fragment comprising the amino acid

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:45.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

> (a) a process comprising the steps of:

sequence from amino acid 66 to amino acid 75 of SEQ ID NO:46.

- preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - SEQ ID NO:45, but excluding the poly(A) tail at the (aa) 3' end of SEQ ID NO:45; and
  - the nucleotide sequence of the cDNA insert of clone vc47\_1 deposited with the ATCC under accession number 98886;
- hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- isolating the DNA polynucleotides detected with the (iii) probe(s);

30

25

10

15

and

5

10

15

20

25

30

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:45, but excluding the poly(A) tail at the 3' end of SEQ ID NO:45; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vc47\_1 deposited with the ATCC under accession number 98886;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:45, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:45 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:45, but excluding the poly(A) tail at the 3' end of SEQ ID NO:45. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:45 from nucleotide 1922 to nucleotide 2350, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:45 from nucleotide 1922 to nucleotide 2350, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:45 from nucleotide 1922 to nucleotide 2350. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:45 from nucleotide 2237 to nucleotide 2350, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:45 from nucleotide 2237 to nucleotide 2350, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:45 from nucleotide 2237 to nucleotide 2350.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:46;

(b) a fragment of the amino acid sequence of SEQ ID NO:46, the fragment comprising eight contiguous amino acids of SEQ ID NO:46; and

- (c) the amino acid sequence encoded by the cDNA insert of clone vc47\_1 deposited with the ATCC under accession number 98886;
- 5 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:46. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:46, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46 having biological activity, the fragment comprising the amino acid sequence from amino acid 66 to amino acid 75 of SEQ ID NO:46.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:47;

20

25

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:47 from nucleotide 111 to nucleotide 1337;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:47 from nucleotide 246 to nucleotide 1337;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc54\_1 deposited with the ATCC under accession number 98886;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc54\_1 deposited with the ATCC under accession number 98886;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc54\_1 deposited with the ATCC under accession number 98886;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc54\_1 deposited with the ATCC under accession number 98886;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:48;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:48;

- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:47.

5

15

20

25

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:47 from nucleotide 111 to nucleotide 1337; the nucleotide sequence of SEQ ID NO:47 from nucleotide 246 to nucleotide 1337; the nucleotide sequence of the full-length protein coding sequence of clone vc54\_1 deposited with the ATCC under accession number 98886; or the nucleotide sequence of a mature protein coding sequence of clone vc54\_1 deposited with the ATCC under accession number 98886. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc54\_1 deposited with the ATCC under accession number 98886. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:48, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48 having biological activity, the fragment comprising the amino acid sequence from amino acid 199 to amino acid 208 of SEQ ID NO:48.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:47.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

	(i)	preparing one or more polynucleotide probes that hybridize	
		degrees C to a nucleotide sequence selected from the group	
	consisting of:		
		(aa) SEQ ID NO:47, but excluding the poly(A) tail at the	
5	3' end o	of SEQ ID NO:47; and	
		(ab) the nucleotide sequence of the cDNA insert of clone	
	vc54_1	deposited with the ATCC under accession number 98886;	
	(ii)	hybridizing said probe(s) to human genomic DNA in	
	conditions at least as stringent as 4X SSC at 50 degrees C; and		
10	(iii)	isolating the DNA polynucleotides detected with the	
	probe(s);		
	and		
	(b) a proces	ss comprising the steps of:	
	(i) ]	preparing one or more polynucleotide primers that	
15	hybridize in 6X	SSC at 65 degrees C to a nucleotide sequence selected from	
	the group consisting of:		
	(	(ba) SEQ ID NO:47, but excluding the poly(A) tail at the	
	3' end o	f SEQ ID NO:47; and	
	(	bb) the nucleotide sequence of the cDNA insert of clone	
20	vc54_1 c	deposited with the ATCC under accession number 98886;	
		hybridizing said primer(s) to human genomic DNA in	
	conditions at least as stringent as 4X SSC at 50 degrees C;		
		implifying human DNA sequences; and	
		solating the polynucleotide products of step (b)(iii).	
25		isolated according to the above process comprises a	
		nding to the cDNA sequence of SEQ ID NO:47, and	
		nucleotide sequence corresponding to the 5' end of SEQ	
		ence corresponding to the 3' end of SEQ ID NO:47, but	
2.0		the 3' end of SEQ ID NO:47. Also preferably the	
30	polynucleotide isolated according to the above process comprises a nucleotide sequence		
		juence of SEQ ID NO:47 from nucleotide 111 to nucleotide	
		sly from a nucleotide sequence corresponding to the 5' end	
of said sequence of SEQ ID NO:47 from nucleotide 111 to nucleotide 1337, to a nu			

sequence corresponding to the 3' end of said sequence of SEQ ID NO:47 from nucleotide

111 to nucleotide 1337. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:47 from nucleotide 246 to nucleotide 1337, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:47 from nucleotide 246 to nucleotide 1337, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:47 from nucleotide 246 to nucleotide 1337.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10

- (a) the amino acid sequence of SEQ ID NO:48;
- (b) a fragment of the amino acid sequence of SEQ ID NO:48, the fragment comprising eight contiguous amino acids of SEQ ID NO:48; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc54\_1 deposited with the ATCC under accession number 98886;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:48. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:48, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48 having biological activity, the fragment comprising the amino acid sequence from amino acid 199 to amino acid 208 of SEQ ID NO:48.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:49;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:49 from nucleotide 189 to nucleotide 1637;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:49 from nucleotide 270 to nucleotide 1637;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc57\_1 deposited with the ATCC under accession number 98886;

 (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc57\_1 deposited with the ATCC under accession number 98886;

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc57\_1 deposited with the ATCC under accession number 98886;

5

10

15

20

25

30

- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc57\_1 deposited with the ATCC under accession number 98886;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:50;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:50 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:50;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:49.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:49 from nucleotide 189 to nucleotide 1637; the nucleotide sequence of SEQ ID NO:49 from nucleotide 270 to nucleotide 1637; the nucleotide sequence of the full-length protein coding sequence of clone vc57\_1 deposited with the ATCC under accession number 98886; or the nucleotide sequence of a mature protein coding sequence of clone vc57\_1 deposited with the ATCC under accession number 98886. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc57\_1 deposited with the ATCC under accession number 98886. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:50 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:50, or a polynucleotide

encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:50 having biological activity, the fragment comprising the amino acid sequence from amino acid 236 to amino acid 245 of SEQ ID NO:50.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:49.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:49, but excluding the poly(A) tail at the 3' end of SEQ ID NO:49; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vc57\_1 deposited with the ATCC under accession number 98886;
  - (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
  - (iii) isolating the DNA polynucleotides detected with the probe(s);
- 20 and

5

10

15

25

30

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:49, but excluding the poly(A) tail at the 3' end of SEQ ID NO:49; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vc57\_1 deposited with the ATCC under accession number 98886;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:49, and

extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:49 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:49, but excluding the poly(A) tail at the 3' end of SEQ ID NO:49. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:49 from nucleotide 189 to nucleotide 1637, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:49 from nucleotide 189 to nucleotide 1637, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:49 from nucleotide 189 to nucleotide 1637. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:49 from nucleotide 270 to nucleotide 1637, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:49 from nucleotide 270 to nucleotide 1637, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:49 from nucleotide 270 to nucleotide 1637.

10

20

25

30

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:50;
- (b) a fragment of the amino acid sequence of SEQ ID NO:50, the fragment comprising eight contiguous amino acids of SEQ ID NO:50; and
  - (c) the amino acid sequence encoded by the cDNA insert of clone vc57\_1 deposited with the ATCC under accession number 98886;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:50. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:50 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:50, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:50 having biological activity, the fragment comprising the amino acid sequence from amino acid 236 to amino acid 245 of SEQ ID NO:50.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:51;

5

10

15

20

25

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:51 from nucleotide 15 to nucleotide 1934;

- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:51 from nucleotide 1704 to nucleotide 1934;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone ve13\_1 deposited with the ATCC under accession number 98886;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone ve13\_1 deposited with the ATCC under accession number 98886;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone ve13\_1 deposited with the ATCC under accession number 98886;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone ve13\_1 deposited with the ATCC under accession number 98886;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:52;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:52 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:52;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of(a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:51.
- Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:51 from nucleotide 15 to nucleotide 1934; the nucleotide sequence of SEQ ID NO:51 from nucleotide 1704 to nucleotide 1934; the nucleotide sequence of the full-length protein coding sequence of clone ve13\_1 deposited with the ATCC under accession number 98886; or the nucleotide sequence of a mature protein coding sequence of clone

ve13\_1 deposited with the ATCC under accession number 98886. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone ve13\_1 deposited with the ATCC under accession number 98886.

In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:52 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:52, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:52 having biological activity, the fragment comprising the amino acid sequence from amino acid 315 to amino acid 324 of SEQ ID NO:52.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:51.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

15

20

25

30

10

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:51, but excluding the poly(A) tail at the 3' end of SEQ ID NO:51; and
  - (ab) the nucleotide sequence of the cDNA insert of cloneve13\_1 deposited with the ATCC under accession number 98886;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:51, but excluding the poly(A) tail at the 3' end of SEQ ID NO:51; and

5

10

15

20

25

(bb) the nucleotide sequence of the cDNA insert of clone ve13\_1 deposited with the ATCC under accession number 98886;

- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:51, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:51 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:51, but excluding the poly(A) tail at the 3' end of SEQ ID NO:51. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:51 from nucleotide 15 to nucleotide 1934, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:51 from nucleotide 15 to nucleotide 1934, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:51 from nucleotide 15 to nucleotide 1934. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:51 from nucleotide 1704 to nucleotide 1934, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:51 from nucleotide 1704 to nucleotide 1934, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:51 from nucleotide 1704 to nucleotide 1934.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:52;
- (b) a fragment of the amino acid sequence of SEQ ID NO:52, the fragment comprising eight contiguous amino acids of SEQ ID NO:52; and
- (c) the amino acid sequence encoded by the cDNA insert of clone ve13\_1 deposited with the ATCC under accession number 98886;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:52. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:52 having biological activity, the fragment preferably

comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:52, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:52 having biological activity, the fragment comprising the amino acid sequence from amino acid 315 to amino acid 324 of SEQ ID NO:52.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

5

15

20

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:53;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:53 from nucleotide 240 to nucleotide 503;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:53 from nucleotide 318 to nucleotide 503;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone ve16\_1 deposited with the ATCC under accession number 98886;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone ve16\_1 deposited with the ATCC under accession number 98886;
  - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone ve16\_1 deposited with the ATCC under accession number 98886;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone ve16\_1 deposited with the ATCC under accession number 98886;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:54;
  - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:54 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:54;
  - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
  - (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
  - (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:53.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:53 from nucleotide 240 to nucleotide 503; the nucleotide sequence of the full-length protein coding sequence of clone ve16\_1 deposited with the ATCC under accession number 98886; or the nucleotide sequence of a mature protein coding sequence of clone ve16\_1 deposited with the ATCC under accession number 98886. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone ve16\_1 deposited with the ATCC under accession number 98886. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:54 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:54, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:54 having biological activity, the fragment comprising the amino acid sequence from amino acid 39 to amino acid 48 of SEQ ID NO:54.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:53.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:53, but excluding the poly(A) tail at the 3' end of SEQ ID NO:53; and
  - (ab) the nucleotide sequence of the cDNA insert of clone ve16\_1 deposited with the ATCC under accession number 98886;
  - (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
  - (iii) isolating the DNA polynucleotides detected with the probe(s);

10

15

20

and

5

10

15

20

25

30

(b) a process comprising the steps of:

- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:53, but excluding the poly(A) tail at the 3' end of SEQ ID NO:53; and
  - (bb) the nucleotide sequence of the cDNA insert of clone ve16\_1 deposited with the ATCC under accession number 98886;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:53, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:53 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:53, but excluding the poly(A) tail at the 3' end of SEQ ID NO:53. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:53 from nucleotide 240 to nucleotide 503, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:53 from nucleotide 240 to nucleotide 503, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:53 from nucleotide 240 to nucleotide 503. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:53 from nucleotide 318 to nucleotide 503, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:53 from nucleotide 318 to nucleotide 503, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:53 from nucleotide 318 to nucleotide 503.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:54;

(b) a fragment of the amino acid sequence of SEQ ID NO:54, the fragment comprising eight contiguous amino acids of SEQ ID NO:54; and

- (c) the amino acid sequence encoded by the cDNA insert of clone ve16\_1 deposited with the ATCC under accession number 98886;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:54. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:54 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:54, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:54 having biological activity, the fragment comprising the amino acid sequence from amino acid 39 to amino acid 48 of SEQ ID NO:54.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:55;

20 .

25

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:55 from nucleotide 11 to nucleotide 1063;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:55 from nucleotide 71 to nucleotide 1063;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vf3\_1 deposited with the ATCC under accession number 98886;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vf3\_1 deposited with the ATCC under accession number 98886;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vf3\_1 deposited with the ATCC under accession number 98886;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vf3\_1 deposited with the ATCC under accession number 98886;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:56;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:56;

- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- 10 (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:55.

5

15

20

25

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:55 from nucleotide 11 to nucleotide 1063; the nucleotide sequence of SEQ ID NO:55 from nucleotide 71 to nucleotide 1063; the nucleotide sequence of the full-length protein coding sequence of clone vf3\_1 deposited with the ATCC under accession number 98886; or the nucleotide sequence of a mature protein coding sequence of clone vf3\_1 deposited with the ATCC under accession number 98886. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vf3\_1 deposited with the ATCC under accession number 98886. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:56, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56 having biological activity, the fragment comprising the amino acid sequence from amino acid 170 to amino acid 179 of SEQ ID NO:56.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:55.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

	(i) preparing one or more polynucleotide probes that hybridiz	ze
	in 6X SSC at 65 degrees C to a nucleotide sequence selected from the grou	ıp
	consisting of:	
	(aa) SEQ ID NO:55, but excluding the poly(A) tail at th	ıe
5	3' end of SEQ ID NO:55; and	
	(ab) the nucleotide sequence of the cDNA insert of clor	ıe
	vf3_1 deposited with the ATCC under accession number 98886;	;
	(ii) hybridizing said probe(s) to human genomic DNA i	in
	conditions at least as stringent as 4X SSC at 50 degrees C; and	
10	(iii) isolating the DNA polynucleotides detected with the	ıe
	probe(s);	
	and	
	(b) a process comprising the steps of:	
	(i) preparing one or more polynucleotide primers that	at
15	hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from	n
	the group consisting of:	
	(ba) SEQ ID NO:55, but excluding the poly(A) tail at th	ıe
	3' end of SEQ ID NO:55; and	
	(bb) the nucleotide sequence of the cDNA insert of clon	
20	vf3_1 deposited with the ATCC under accession number 98886;	
	(ii) hybridizing said primer(s) to human genomic DNA i	n
	conditions at least as stringent as 4X SSC at 50 degrees C;	
	(iii) amplifying human DNA sequences; and	
	(iv) isolating the polynucleotide products of step (b)(iii).	
25	Preferably the polynucleotide isolated according to the above process comprises	
	nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:55, and	
	extending contiguously from a nucleotide sequence corresponding to the 5' end of SEC	
	ID NO:55 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:55, but	
	excluding the poly(A) tail at the 3' end of SEQ ID NO:55. Also preferably the	
30	polynucleotide isolated according to the above process comprises a nucleotide sequence	
	corresponding to the cDNA sequence of SEQ ID NO:55 from nucleotide 11 to nucleotid	
	1063, and extending contiguously from a nucleotide sequence corresponding to the 5' en	d

of said sequence of SEQ ID NO:55 from nucleotide 11 to nucleotide 1063, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:55 from nucleotide

11 to nucleotide 1063. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:55 from nucleotide 71 to nucleotide 1063, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:55 from nucleotide 71 to nucleotide 1063, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:55 from nucleotide 71 to nucleotide 1063.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10

25

30

5

- (a) the amino acid sequence of SEQ ID NO:56;
- (b) a fragment of the amino acid sequence of SEQ ID NO:56, the fragment comprising eight contiguous amino acids of SEQ ID NO:56; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vf3\_1 deposited with the ATCC under accession number 98886;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:56. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:56, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56 having biological activity, the fragment comprising the amino acid sequence from amino acid 170 to amino acid 179 of SEQ ID NO:56.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:57;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:57 from nucleotide 542 to nucleotide 886;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:57 from nucleotide 755 to nucleotide 886;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vj2\_1 deposited with the ATCC under accession number 98886;

5

10

15

20

25

30

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vj2\_1 deposited with the ATCC under accession number 98886;

- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vj2\_1 deposited with the ATCC under accession number 98886;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vj2\_1 deposited with the ATCC under accession number 98886;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:58;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:58;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:57.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:57 from nucleotide 542 to nucleotide 886; the nucleotide sequence of SEQ ID NO:57 from nucleotide 755 to nucleotide 886; the nucleotide sequence of the full-length protein coding sequence of clone vj2\_1 deposited with the ATCC under accession number 98886; or the nucleotide sequence of a mature protein coding sequence of clone vj2\_1 deposited with the ATCC under accession number 98886. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vj2\_1 deposited with the ATCC under accession number 98886. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:58, or a polynucleotide

encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58 having biological activity, the fragment comprising the amino acid sequence from amino acid 52 to amino acid 61 of SEQ ID NO:58.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:57.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:57, but excluding the poly(A) tail at the 3' end of SEQ ID NO:57; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vj2\_1 deposited with the ATCC under accession number 98886;
  - (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
  - (iii) isolating the DNA polynucleotides detected with the probe(s);
- 20 and

5

10

15

25

30

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:57, but excluding the poly(A) tail at the 3' end of SEQ ID NO:57; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vj2\_1 deposited with the ATCC under accession number 98886;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:57, and

extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:57 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:57, but excluding the poly(A) tail at the 3' end of SEQ ID NO:57. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:57 from nucleotide 542 to nucleotide 886, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:57 from nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:57 from nucleotide 542 to nucleotide 886. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:57 from nucleotide 886, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:57 from nucleotide 755 to nucleotide 886, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:57 from nucleotide 755 to nucleotide 886, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:57 from nucleotide 755 to nucleotide 886.

10

15

20

25

30

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:58;
- (b) a fragment of the amino acid sequence of SEQ ID NO:58, the fragment comprising eight contiguous amino acids of SEQ ID NO:58; and
  - (c) the amino acid sequence encoded by the cDNA insert of clone vj2\_1 deposited with the ATCC under accession number 98886;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:58. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:58, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58 having biological activity, the fragment comprising the amino acid sequence from amino acid 52 to amino acid 61 of SEQ ID NO:58.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:59;

5

10

15

20

25

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:59 from nucleotide 30 to nucleotide 344;

- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:59 from nucleotide 84 to nucleotide 344:
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vp7\_1 deposited with the ATCC under accession number 98886;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vp7\_1 deposited with the ATCC under accession number 98886;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vp7\_1 deposited with the ATCC under accession number 98886;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vp7\_1 deposited with the ATCC under accession number 98886;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:60;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:60 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:60;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:59.
- Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:59 from nucleotide 30 to nucleotide 344; the nucleotide sequence of SEQ ID NO:59 from nucleotide 84 to nucleotide 344; the nucleotide sequence of the full-length protein coding sequence of clone vp7\_1 deposited with the ATCC under accession number 98886; or the nucleotide sequence of a mature protein coding sequence of clone vp7\_1 deposited

with the ATCC under accession number 98886. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vp7\_1 deposited with the ATCC under accession number 98886. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:60 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:60, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:60 having biological activity, the fragment comprising the amino acid sequence from amino acid 47 to amino acid 56 of SEQ ID NO:60.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:59.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

15

20

25

30

10

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:59, but excluding the poly(A) tail at the 3' end of SEQ ID NO:59; and
  - (ab) the nucleotide sequence of the cDNA insert of clonevp7\_1 deposited with the ATCC under accession number 98886;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:59, but excluding the poly(A) tail at the 3' end of SEQ ID NO:59; and

(bb) the nucleotide sequence of the cDNA insert of clone vp7\_1 deposited with the ATCC under accession number 98886;

- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and

5

10

15

20

25

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:59, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:59 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:59, but excluding the poly(A) tail at the 3' end of SEQ ID NO:59. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:59 from nucleotide 30 to nucleotide 344, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:59 from nucleotide 30 to nucleotide 344, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:59 from nucleotide 30 to nucleotide 344. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:59 from nucleotide 84 to nucleotide 344, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:59 from nucleotide 84 to nucleotide 344, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:59 from nucleotide 84 to nucleotide 344.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:60;
- (b) a fragment of the amino acid sequence of SEQ ID NO:60, the fragment comprising eight contiguous amino acids of SEQ ID NO:60; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vp7\_1 deposited with the ATCC under accession number 98886; the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:60. In further preferred

embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:60 having biological activity, the fragment preferably

comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:60, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:60 having biological activity, the fragment comprising the amino acid sequence from amino acid 47 to amino acid 56 of SEQ ID NO:60.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

5

10

15

20

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:61:
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:61 from nucleotide 23 to nucleotide 757;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:61 from nucleotide 119 to nucleotide 757;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vp8\_1 deposited with the ATCC under accession number 98886;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vp8\_1 deposited with the ATCC under accession number 98886;
  - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vp8\_1 deposited with the ATCC under accession number 98886;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vp8\_1 deposited with the ATCC under accession number 98886;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:62;
  - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:62 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:62;
  - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
  - $\begin{tabular}{ll} (k) & a polynucleotide which encodes a species homologue of the protein of (h) or (i) above; \end{tabular}$
  - (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:61.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID 5 NO:61 from nucleotide 23 to nucleotide 757; the nucleotide sequence of SEQ ID NO:61 from nucleotide 119 to nucleotide 757; the nucleotide sequence of the full-length protein coding sequence of clone vp8\_1 deposited with the ATCC under accession number 98886; or the nucleotide sequence of a mature protein coding sequence of clone vp8\_1 deposited with the ATCC under accession number 98886. In other preferred embodiments, the `10 polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vp8\_1 deposited with the ATCC under accession number 98886. preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:62 having biological activity, the fragment preferably comprising eight (more preferably twenty, 15 most preferably thirty) contiguous amino acids of SEQ ID NO:62, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:62 having biological activity, the fragment comprising the amino acid sequence from amino acid 117 to amino acid 126 of SEO ID NO:62.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 20 ID NO:61.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:61, but excluding the poly(A) tail at the 3' end of SEQ ID NO:61; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vp8\_1 deposited with the ATCC under accession number 98886;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

5

10

15

20

25

30

(b) a process comprising the steps of:

- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:61, but excluding the poly(A) tail at the 3' end of SEQ ID NO:61; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vp8\_1 deposited with the ATCC under accession number 98886;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:61, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:61 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:61, but excluding the poly(A) tail at the 3' end of SEQ ID NO:61. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:61 from nucleotide 23 to nucleotide 757, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:61 from nucleotide 23 to nucleotide 757, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:61 from nucleotide 23 to nucleotide 757. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:61 from nucleotide 119 to nucleotide 757, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:61 from nucleotide 119 to nucleotide 757, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:61 from nucleotide 119 to nucleotide 757.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:62;

(b) a fragment of the amino acid sequence of SEQ ID NO:62, the fragment comprising eight contiguous amino acids of SEQ ID NO:62; and

- (c) the amino acid sequence encoded by the cDNA insert of clone vp8\_1 deposited with the ATCC under accession number 98886;
- 5 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:62. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:62 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:62, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:62 having biological activity, the fragment comprising the amino acid sequence from amino acid 117 to amino acid 126 of SEQ ID NO:62.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:63;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:63 from nucleotide 1048 to nucleotide 3726;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vb22\_1 deposited with the ATCC under accession number 98933;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vb22\_1 deposited with the ATCC under accession number 98933;

25

20

- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vb22\_1 deposited with the ATCC under accession number 98933;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vb22\_1 deposited with the ATCC under accession number 98933;

- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:64;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:64;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above;

- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.;
- (k) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h); and
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h) and that has a length that is at least 25% of the length of SEQ ID NO:63.

10 Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:63 from nucleotide 1048 to nucleotide 3726; the nucleotide sequence of the full-length protein coding sequence of clone vb22\_1 deposited with the ATCC under accession number 98933; or the nucleotide sequence of a mature protein coding sequence of clone vb22\_1 deposited with the ATCC under accession number 98933. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vb22\_1 deposited with the ATCC under accession number 98933.

5

20

30

In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:64, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64 having biological activity, the fragment comprising the amino acid sequence from amino acid 441 to amino acid 450 of SEQ ID NO:64.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 25 ID NO:63.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:63, but excluding the poly(A) tail at the 3' end of SEQ ID NO:63; and

(ab) the nucleotide sequence of the cDNA insert of clonevb22\_1 deposited with the ATCC under accession number 98933;

- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

5

10

15

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:63, but excluding the poly(A) tail at the 3' end of SEQ ID NO:63; and
  - (bb) the nucleotide sequence of the cDNA insert of clonevb22\_1 deposited with the ATCC under accession number 98933;
  - (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
    - (iii) amplifying human DNA sequences; and
    - (iv) isolating the polynucleotide products of step (b)(iii).
- Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:63, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:63 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:63, but excluding the poly(A) tail at the 3' end of SEQ ID NO:63. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:63 from nucleotide 1048 to nucleotide 3726, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:63 from nucleotide 3726, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:63 from nucleotide 1048 to nucleotide 3726.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:64;

(b) a fragment of the amino acid sequence of SEQ ID NO:64, the fragment comprising eight contiguous amino acids of SEQ ID NO:64; and

- (c) the amino acid sequence encoded by the cDNA insert of clone vb22\_1 deposited with the ATCC under accession number 98933;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:64. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:64, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64 having biological activity, the fragment comprising the amino acid sequence from amino acid 441 to amino acid 450 of SEQ ID NO:64.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:65;

20

25

30

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:65 from nucleotide 134 to nucleotide 667;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:65 from nucleotide 191 to nucleotide 667;

- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc48\_1 deposited with the ATCC under accession number 98933;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc48\_1 deposited with the ATCC under accession number 98933;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc48\_1 deposited with the ATCC under accession number 98933;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc48\_1 deposited with the ATCC under accession number 98933;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:66;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:66 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:66;

- (j) a polynucleotide which is an allelic variant of a polynucleotide of(a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above ;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:65.

5

15

20

25

30

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:65 from nucleotide 134 to nucleotide 667; the nucleotide sequence of SEQ ID NO:65 from nucleotide 191 to nucleotide 667; the nucleotide sequence of the full-length protein coding sequence of clone vc48\_1 deposited with the ATCC under accession number 98933; or the nucleotide sequence of a mature protein coding sequence of clone vc48\_1 deposited with the ATCC under accession number 98933. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc48\_1 deposited with the ATCC under accession number 98933. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:66 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:66, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:66 having biological activity, the fragment comprising the amino acid sequence from amino acid 84 to amino acid 93 of SEQ ID NO:66.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:65.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

PCT/US99/19351 WO 00/11015

	(i) preparing one or more polynucleotide pr	obes that hybridize
	in 6X SSC at 65 degrees C to a nucleotide sequence selec	<del>-</del>
	, consisting of:	•
	(aa) SEQ ID NO:65, but excluding the	poly(A) tail at the
5		
	(ab) the nucleotide sequence of the cD	NA insert of clone
	vc48_1 deposited with the ATCC under accessi	
	(ii) hybridizing said probe(s) to human	genomic DNA in
	conditions at least as stringent as 4X SSC at 50 degrees	C; and
10	(iii) isolating the DNA polynucleotides d	etected with the
	probe(s);	
	and ·	
	(b) a process comprising the steps of:	
	(i) preparing one or more polynucleoti	de primers that
hybridize in 6X SSC at 65 degrees C to a nucleotide sequence s		ence selected from
	the group consisting of:	
	(ba) SEQ ID NO:65, but excluding the	poly(A) tail at the
	3' end of SEQ ID NO:65; and	
	(bb) the nucleotide sequence of the cDl	NA insert of clone
20	0 vc48_1 deposited with the ATCC under accession	on number 98933;
	(ii) hybridizing said primer(s) to human g	
	conditions at least as stringent as 4X SSC at 50 degrees	
	(iii) amplifying human DNA sequences; and	
	(iv) isolating the polynucleotide products of	
25	provided isolated according to the above prod	ess comprises a
	nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:65, and	
	extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ	
	ID NO:65 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:65, but	
30	excluding the poly(A) tail at the 3' end of SEQ ID NO:65. Also	preferably the
	polynucleotide isolated according to the above process comprises a nucleotide sequence	
	corresponding to the cDNA sequence of SEQ ID NO:65 from nucleotide 134 to nucleotide	
	667, and extending contiguously from a nucleotide sequence corresponding to the 5' end	
	of said sequence of SEQ ID NO:65 from nucleotide 134 to nucleotide 667	<sup>7</sup> , to a nucleotide

sequence corresponding to the 3' end of said sequence of SEQ ID NO:65 from nucleotide

134 to nucleotide 667. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:65 from nucleotide 191 to nucleotide 667, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:65 from nucleotide 191 to nucleotide 667, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:65 from nucleotide 191 to nucleotide 667.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10

- (a) the amino acid sequence of SEQ ID NO:66;
- (b) a fragment of the amino acid sequence of SEQ ID NO:66, the fragment comprising eight contiguous amino acids of SEQ ID NO:66; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc48\_1 deposited with the ATCC under accession number 98933;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:66. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:66 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:66, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:66 having biological activity, the fragment comprising the amino acid sequence from amino acid 84 to amino acid 93 of SEQ ID NO:66.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

25

30

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:67;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:67 from nucleotide 65 to nucleotide 457;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:67 from nucleotide 158 to nucleotide 457;
- (d) a polynucleotide comprising the nucleotide sequence of the fulllength protein coding sequence of clone vp3\_1 deposited with the ATCC under accession number 98933;

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vp3\_1 deposited with the ATCC under accession number 98933;

(f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vp3\_1 deposited with the ATCC under accession number 98933;

5

10

15

20

25

30

- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vp3\_1 deposited with the ATCC under accession number 98933;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:68;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:68 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:68;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein
   of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:67.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:67 from nucleotide 65 to nucleotide 457; the nucleotide sequence of SEQ ID NO:67 from nucleotide 158 to nucleotide 457; the nucleotide sequence of the full-length protein coding sequence of clone vp3\_1 deposited with the ATCC under accession number 98933; or the nucleotide sequence of a mature protein coding sequence of clone vp3\_1 deposited with the ATCC under accession number 98933. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vp3\_1 deposited with the ATCC under accession number 98933. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:68 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:68, or a polynucleotide

encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:68 having biological activity, the fragment comprising the amino acid sequence from amino acid 60 to amino acid 69 of SEQ ID NO:68.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 5 ID NO:67.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:67, but excluding the poly(A) tail at the 3' end of SEQ ID NO:67; and
  - (ab) the nucleotide sequence of the cDNA insert of clone vp3\_1 deposited with the ATCC under accession number 98933;
  - (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
  - (iii) isolating the DNA polynucleotides detected with the probe(s);
- 20 and

10

15

25

30

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:67, but excluding the poly(A) tail at the 3' end of SEQ ID NO:67; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vp3\_1 deposited with the ATCC under accession number 98933;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:67, and

extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:67 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:67, but excluding the poly(A) tail at the 3' end of SEQ ID NO:67. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:67 from nucleotide 65 to nucleotide 457, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:67 from nucleotide 457, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:67 from nucleotide 65 to nucleotide 457. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:67 from nucleotide 158 to nucleotide 457, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:67 from nucleotide 158 to nucleotide 457, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:67 from nucleotide 158 to nucleotide 457, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:67 from nucleotide 158 to nucleotide 457.

10

15

20

25

30

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:68;
- (b) a fragment of the amino acid sequence of SEQ ID NO:68, the fragment comprising eight contiguous amino acids of SEQ ID NO:68; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vp3\_1 deposited with the ATCC under accession number 98933;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:68. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:68 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:68, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:68 having biological activity, the fragment comprising the amino acid sequence from amino acid 60 to amino acid 69 of SEQ ID NO:68.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:69;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:69 from nucleotide 29 to nucleotide 1387;

- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:69 from nucleotide 113 to nucleotide 1387;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vc61\_1 deposited with the ATCC under accession number 207012;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vc61\_1 deposited with the ATCC under accession number 207012;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vc61\_1 deposited with the ATCC under accession number 207012;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vc61\_1 deposited with the ATCC under accession number 207012;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:70;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:70 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:70;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:69.
- Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:69 from nucleotide 29 to nucleotide 1387; the nucleotide sequence of SEQ ID NO:69 from nucleotide 113 to nucleotide 1387; the nucleotide sequence of the full-length protein coding sequence of clone vc61\_1 deposited with the ATCC under accession number 207012; or the nucleotide sequence of a mature protein coding sequence of clone vc61\_1

5

10

15

20

25

deposited with the ATCC under accession number 207012. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vc61\_1 deposited with the ATCC under accession number 207012. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:70 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:70, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:70 having biological activity, the fragment comprising the amino acid sequence from amino acid 221 to amino acid 230 of SEQ ID NO:70.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:69.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

15

20

25

30

10

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:69, but excluding the poly(A) tail at the 3' end of SEQ ID NO:69; and
  - (ab) the nucleotide sequence of the cDNA insert of clonevc61\_1 deposited with the ATCC under accession number 207012;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:69, but excluding the poly(A) tail at the 3' end of SEQ ID NO:69; and

(bb) the nucleotide sequence of the cDNA insert of clone vc61\_1 deposited with the ATCC under accession number 207012;

- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and

5

10

15

20

25

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:69, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:69 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:69 , but excluding the poly(A) tail at the 3' end of SEQ ID NO:69. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:69 from nucleotide 29 to nucleotide 1387, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:69 from nucleotide 29 to nucleotide 1387, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:69 from nucleotide 29 to nucleotide 1387. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:69 from nucleotide 113 to nucleotide 1387, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:69 from nucleotide 113 to nucleotide 1387, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:69 from nucleotide 113 to nucleotide 1387.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:70;
- (b) a fragment of the amino acid sequence of SEQ ID NO:70, the fragment comprising eight contiguous amino acids of SEQ ID NO:70; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc61\_1 deposited with the ATCC under accession number 207012; the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:70. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:70 having biological activity, the fragment preferably

comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:70, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:70 having biological activity, the fragment comprising the amino acid sequence from amino acid 221 to amino acid 230 of SEQ ID NO:70.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

5

10

15

20

25

30

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:71;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:71 from nucleotide 44 to nucleotide 1513;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:71 from nucleotide 92 to nucleotide 1513;
  - (d) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:71 from nucleotide 1 to nucleotide 458;
  - (e) a polynucleotide comprising the nucleotide sequence of the fulllength protein coding sequence of clone vp15\_1 deposited with the ATCC under accession number 207012;
    - (f) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vp15\_1 deposited with the ATCC under accession number 207012;
    - (g) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vp15\_1 deposited with the ATCC under accession number 207012;
    - (h) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vp15\_1 deposited with the ATCC under accession number 207012;
    - (i) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:72;
    - (j) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:72 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:72;
    - (k) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(h) above;
    - (l) a polynucleotide which encodes a species homologue of the protein of (i) or (j) above ;

5

10

15

20

30

(m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(j); and

(n) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(j) and that has a length that is at least 25% of the length of SEQ ID NO:71.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:71 from nucleotide 44 to nucleotide 1513; the nucleotide sequence of SEQ ID NO:71 from nucleotide 92 to nucleotide 1513; the nucleotide sequence of SEQ ID NO:71 from nucleotide 1 to nucleotide 458; the nucleotide sequence of the full-length protein coding sequence of clone vp15\_1 deposited with the ATCC under accession number 207012; or the nucleotide sequence of a mature protein coding sequence of clone vp15\_1 deposited with the ATCC under accession number 207012. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vp15\_1 deposited with the ATCC under accession number 207012. In yet other preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:72 from amino acid 1 to amino In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:72 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:72, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:72 having biological activity, the fragment comprising the amino acid sequence from amino acid 240 to amino acid 249 of SEQ ID NO:72.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ 25 ID NO:71.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (aa) SEQ ID NO:71, but excluding the poly(A) tail at the 3' end of SEQ ID NO:71; and

(ab) the nucleotide sequence of the cDNA insert of clone vp15\_1 deposited with the ATCC under accession number 207012;

- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

5

15

20

25

30

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that

  hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from
  the group consisting of:
  - (ba) SEQ ID NO:71, but excluding the poly(A) tail at the 3' end of SEQ ID NO:71; and
  - (bb) the nucleotide sequence of the cDNA insert of clone vp15\_1 deposited with the ATCC under accession number 207012;
  - (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
    - (iii) amplifying human DNA sequences; and
    - (iv) isolating the polynucleotide products of step (b)(iii).
  - Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:71, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:71 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:71, but excluding the poly(A) tail at the 3' end of SEQ ID NO:71. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:71 from nucleotide 44 to nucleotide 1513, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:71 from nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:71 from nucleotide 44 to nucleotide 1513. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:71 from nucleotide 92 to nucleotide 1513, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:71 from nucleotide 92 to nucleotide 1513, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:71 from nucleotide 92 to nucleotide 1513, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:71 from nucleotide 92 to nucleotide 1513, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:71 from nucleotide 92 to nucleotide 1513, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:71 from nuc

said sequence of SEQ ID NO:71 from nucleotide 92 to nucleotide 1513. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:71 from nucleotide 1 to nucleotide 458, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:71 from nucleotide 1 to nucleotide 458, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:71 from nucleotide 1 to nucleotide 458.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:72;

10

15

20

25

- (b) the amino acid sequence of SEQ ID NO:72 from amino acid 1 to amino acid 139;
- (c) a fragment of the amino acid sequence of SEQ ID NO:72, the fragment comprising eight contiguous amino acids of SEQ ID NO:72; and
- (d) the amino acid sequence encoded by the cDNA insert of clone vp15\_1 deposited with the ATCC under accession number 207012;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:72 or the amino acid sequence of SEQ ID NO:72 from amino acid 1 to amino acid 139. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:72 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:72, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:72 having biological activity, the fragment comprising the amino acid sequence from amino acid 240 to amino acid 249 of SEQ ID NO:72.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:73;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:73 from nucleotide 348 to nucleotide 743;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:73 from nucleotide 414 to nucleotide 743:

(d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vp17\_1 deposited with the ATCC under accession number 207012;

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vp17\_1 deposited with the ATCC under accession number 207012:

5

10

15

20

25

30

- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vp17\_1 deposited with the ATCC under accession number 207012;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vp17\_1 deposited with the ATCC under accession number 207012;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:74;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:74 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:74;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:73.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:73 from nucleotide 348 to nucleotide 743; the nucleotide sequence of SEQ ID NO:73 from nucleotide 414 to nucleotide 743; the nucleotide sequence of the full-length protein coding sequence of clone vp17\_1 deposited with the ATCC under accession number 207012; or the nucleotide sequence of a mature protein coding sequence of clone vp17\_1 deposited with the ATCC under accession number 207012. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vp17\_1 deposited with the ATCC under accession number 207012. In further preferred embodiments, the present invention provides a

polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:74 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:74, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:74 having biological activity, the fragment comprising the amino acid sequence from amino acid 61 to amino acid 70 of SEQ ID NO:74.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:73.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

15

- (aa) SEQ ID NO:73, but excluding the poly(A) tail at the 3' end of SEQ ID NO:73; and
- (ab) the nucleotide sequence of the cDNA insert of clone vp17\_1 deposited with the ATCC under accession number 207012;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

25

20

- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:73, but excluding the poly(A) tail at the 3' end of SEQ ID NO:73; and

30

- (bb) the nucleotide sequence of the cDNA insert of clone vp17\_1 deposited with the ATCC under accession number 207012;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:73, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:73 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:73, but excluding the poly(A) tail at the 3' end of SEQ ID NO:73. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:73 from nucleotide 348 to nucleotide 743, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:73 from nucleotide 348 to nucleotide 743, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:73 from nucleotide 348 to nucleotide 743. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:73 from nucleotide 414 to nucleotide 743, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:73 from nucleotide 414 to nucleotide 743, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:73 from nucleotide 414 to nucleotide 743.

10

15

20

30

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:74;
- (b) a fragment of the amino acid sequence of SEQ ID NO:74, the fragment comprising eight contiguous amino acids of SEQ ID NO:74; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vp17\_1 deposited with the ATCC under accession number 207012; the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:74. In further preferred embodiments, the present invention provides a protein comprising a fragment of the

embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:74 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:74, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:74 having biological activity, the fragment comprising the amino acid sequence from amino acid 61 to amino acid 70 of SEQ ID NO:74.

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:75:

5

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:75 from nucleotide 144 to nucleotide 461;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vp19\_1 deposited with the ATCC under accession number 207012;

10

- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vp19\_1 deposited with the ATCC under accession number 207012:
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vp19\_1 deposited with the ATCC under accession number 207012;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vp19\_1 deposited with the ATCC under accession number 207012;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:76;

20

15

- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:76 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:76;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above;

25

- (j) a polynucleotide which encodes a species homologue of the proteinof (g) or (h) above;
- (k) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h); and

30

(l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(h) and that has a length that is at least 25% of the length of SEQ ID NO:75.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:75 from nucleotide 144 to nucleotide 461; the nucleotide sequence of the full-length protein coding sequence of clone vp19\_1 deposited with the ATCC under accession

number 207012; or the nucleotide sequence of a mature protein coding sequence of clone vp19\_1 deposited with the ATCC under accession number 207012. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vp19\_1 deposited with the ATCC under accession number 207012. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:76 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:76, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:76 having biological activity, the fragment comprising the amino acid sequence from amino acid 48 to amino acid 57 of SEQ ID NO:76.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:75.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

20

25

10

- (aa) SEQ ID NO:75, but excluding the poly(A) tail at the 3' end of SEQ ID NO:75; and
- (ab) the nucleotide sequence of the cDNA insert of clone vp19\_1 deposited with the ATCC under accession number 207012;
- (ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and
- (iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

30 (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:75, but excluding the poly(A) tail at the 3' end of SEQ ID NO:75; and

(bb) the nucleotide sequence of the cDNA insert of clone vp19\_1 deposited with the ATCC under accession number 207012;

- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and

5

10

15

20

25

30

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:75, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:75 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:75, but excluding the poly(A) tail at the 3' end of SEQ ID NO:75. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:75 from nucleotide 144 to nucleotide 461, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:75 from nucleotide 461, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:75 from nucleotide 144 to nucleotide 461.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:76;
- (b) a fragment of the amino acid sequence of SEQ ID NO:76, the fragment comprising eight contiguous amino acids of SEQ ID NO:76; and
- (c) the amino acid sequence encoded by the cDNA insert of clonevp19\_1 deposited with the ATCC under accession number 207012;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:76. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:76 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:76, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:76 having biological activity, the fragment comprising the amino acid sequence from amino acid 48 to amino acid 57 of SEQ ID NO:76.

5

10

15

20

25

30

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:77;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:77 from nucleotide 54 to nucleotide 368;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:77 from nucleotide 141 to nucleotide 368;
- (d) a polynucleotide comprising the nucleotide sequence of SEQ ID
   NO:77 from nucleotide 51 to nucleotide 332;
  - (e) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vq1\_1 deposited with the ATCC under accession number 207012;
  - (f) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vq1\_1 deposited with the ATCC under accession number 207012;
  - (g) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vq1\_1 deposited with the ATCC under accession number 207012;
- (h) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vq1\_1 deposited with the ATCC under accession number 207012;
- (i) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:78;
- (j) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:78 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:78;
- (k) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(h) above;
- (l) a polynucleotide which encodes a species homologue of the protein of (i) or (j) above ;
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(j); and

> a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(j) and that has a length that is at least 25% of the length of SEQ ID NO:77.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:77 from nucleotide 54 to nucleotide 368; the nucleotide sequence of SEQ ID NO:77 from nucleotide 141 to nucleotide 368; the nucleotide sequence of SEQ ID NO:77 from nucleotide 51 to nucleotide 332; the nucleotide sequence of the full-length protein coding sequence of clone vq1\_1 deposited with the ATCC under accession number 207012; or the nucleotide sequence of a mature protein coding sequence of clone vq1\_1 deposited with the ATCC under accession number 207012. In other preferred embodiments, the 10 polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vq1\_1 deposited with the ATCC under accession number 207012. In yet other preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:78 from amino acid 1 to amino In further preferred embodiments, the present invention provides a 15 acid 93. polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:78 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:78, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:78 having biological activity, the fragment comprising the amino acid sequence from amino acid 47 to amino acid 56 of SEQ ID NO:78.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:77.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of: 25

- (a) a process comprising the steps of:
- (i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

30

20

- SEQ ID NO:77, but excluding the poly(A) tail at the 3' end of SEQ ID NO:77; and
- the nucleotide sequence of the cDNA insert of clone vq1\_1 deposited with the ATCC under accession number 207012;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

(iii) isolating the DNA polynucleotides detected with the probe(s);

5 and

10

15

20

25

30

- (b) a process comprising the steps of:
- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

(ba) SEQ ID NO:77, but excluding the poly(A) tail at the 3' end of SEQ ID NO:77; and

- (bb) the nucleotide sequence of the cDNA insert of clone vq1\_1 deposited with the ATCC under accession number 207012;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and
  - (iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:77, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:77 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:77, but excluding the poly(A) tail at the 3' end of SEQ ID NO:77. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:77 from nucleotide 54 to nucleotide 368, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:77 from nucleotide 54 to nucleotide 368, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:77 from nucleotide 54 to nucleotide 368. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:77 from nucleotide 141 to nucleotide 368, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:77 from nucleotide 141 to nucleotide 368, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:77 from nucleotide 141 to nucleotide 368. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide

sequence corresponding to the cDNA sequence of SEQ ID NO:77 from nucleotide 51 to nucleotide 332, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:77 from nucleotide 51 to nucleotide 332, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:77 from nucleotide 51 to nucleotide 332.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:78;
- 10 (b) the amino acid sequence of SEQ ID NO:78 from amino acid 1 to amino acid 93;
  - (c) a fragment of the amino acid sequence of SEQ ID NO:78, the fragment comprising eight contiguous amino acids of SEQ ID NO:78; and
- (d) the amino acid sequence encoded by the cDNA insert of clone vq1\_1 deposited with the ATCC under accession number 207012;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:78 or the amino acid sequence of SEQ ID NO:78 from amino acid 1 to amino acid 93. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:78 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:78, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:78 having biological activity, the fragment comprising the amino acid sequence from amino acid 47 to amino acid 56 of SEQ ID NO:78.

20

In one embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:79;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:79 from nucleotide 2 to nucleotide 1018;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:79 from nucleotide 53 to nucleotide 1018;

(d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone vp14\_1 deposited with the ATCC under accession number 207011;

5

- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone vp14\_1 deposited with the ATCC under accession number 207011;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone vp14\_1 deposited with the ATCC under accession number 207011;

10

15

20

25

- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone vp14\_1 deposited with the ATCC under accession number 207011;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:80;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:80 having biological activity, the fragment comprising eight contiguous amino acids of SEQ ID NO:80;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of
   (a)-(g) above;
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above;
- (l) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i); and
- (m) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i) and that has a length that is at least 25% of the length of SEQ ID NO:79.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:79 from nucleotide 2 to nucleotide 1018; the nucleotide sequence of SEQ ID NO:79 from nucleotide 53 to nucleotide 1018; the nucleotide sequence of the full-length protein coding sequence of clone vp14\_1 deposited with the ATCC under accession number 207011; or the nucleotide sequence of a mature protein coding sequence of clone vp14\_1 deposited with the ATCC under accession number 207011. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone vp14\_1 deposited with the ATCC under accession number 207011. In further preferred embodiments, the present invention provides a

polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:80 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:80, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:80 having biological activity, the fragment comprising the amino acid sequence from amino acid 164 to amino acid 173 of SEQ ID NO:80.

Other embodiments provide the gene corresponding to the cDNA sequence of SEQ ID NO:79.

Further embodiments of the invention provide isolated polynucleotides produced according to a process selected from the group consisting of:

(a) a process comprising the steps of:

(i) preparing one or more polynucleotide probes that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:

15

- (aa) SEQ ID NO:79, but excluding the poly(A) tail at the 3' end of SEQ ID NO:79; and
- (ab) the nucleotide sequence of the cDNA insert of clonevp14\_1 deposited with the ATCC under accession number 207011;

(ii) hybridizing said probe(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C; and

(iii) isolating the DNA polynucleotides detected with the probe(s);

and

(b) a process comprising the steps of:

25

20

- (i) preparing one or more polynucleotide primers that hybridize in 6X SSC at 65 degrees C to a nucleotide sequence selected from the group consisting of:
  - (ba) SEQ ID NO:79, but excluding the poly(A) tail at the 3' end of SEQ ID NO:79; and

30

- (bb) the nucleotide sequence of the cDNA insert of clonevp14\_1 deposited with the ATCC under accession number 207011;
- (ii) hybridizing said primer(s) to human genomic DNA in conditions at least as stringent as 4X SSC at 50 degrees C;
  - (iii) amplifying human DNA sequences; and

(iv) isolating the polynucleotide products of step (b)(iii).

Preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:79, and extending contiguously from a nucleotide sequence corresponding to the 5' end of SEQ ID NO:79 to a nucleotide sequence corresponding to the 3' end of SEQ ID NO:79 , but excluding the poly(A) tail at the 3' end of SEQ ID NO:79. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:79 from nucleotide 2 to nucleotide 1018, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:79 from nucleotide 2 to nucleotide 1018, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:79 from nucleotide 2 to nucleotide 1018. Also preferably the polynucleotide isolated according to the above process comprises a nucleotide sequence corresponding to the cDNA sequence of SEQ ID NO:79 from nucleotide 53 to nucleotide 1018, and extending contiguously from a nucleotide sequence corresponding to the 5' end of said sequence of SEQ ID NO:79 from nucleotide 53 to nucleotide 1018, to a nucleotide sequence corresponding to the 3' end of said sequence of SEQ ID NO:79 from nucleotide 53 to nucleotide 1018.

10

15

20

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:80;
- (b) a fragment of the amino acid sequence of SEQ ID NO:80, the fragment comprising eight contiguous amino acids of SEQ ID NO:80; and
- vp14\_1 deposited with the ATCC under accession number 207011; the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:80. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:80 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) contiguous amino acids of SEQ ID NO:80, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:80 having biological activity, the fragment comprising the amino acid sequence from amino acid 164 to amino acid 173 of SEQ ID NO:80.

In certain preferred embodiments, the polynucleotide is operably linked to an expression control sequence. The invention also provides a host cell, including bacterial, yeast, insect and mammalian cells, transformed with such polynucleotide compositions. Also provided by the present invention are organisms that have enhanced, reduced, or 5 modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein.

Processes are also provided for producing a protein, which comprise:

- growing a culture of the host cell transformed with such polynucleotide compositions in a suitable culture medium; and
- purifying the protein from the culture. The protein produced according to such methods is also provided by the present invention.

Protein compositions of the present invention may further comprise a pharmaceutically acceptable carrier. Compositions comprising an antibody which specifically reacts with such protein are also provided by the present invention.

Methods are also provided for preventing, treating or ameliorating a medical condition which comprises administering to a mammalian subject a therapeutically effective amount of a composition comprising a protein of the present invention and a pharmaceutically acceptable carrier.

20

10

15

(b)

# BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A and 1B are schematic representations of the pED6 and pNOTs vectors, respectively, used for deposit of clones disclosed herein.

25

30

## **DETAILED DESCRIPTION**

# **ISOLATED PROTEINS AND POLYNUCLEOTIDES**

Nucleotide and amino acid sequences, as presently determined, are reported below for each clone and protein disclosed in the present application. The nucleotide sequence of each clone can readily be determined by sequencing of the deposited clone in accordance with known methods. The predicted amino acid sequence (both full-length and mature forms) can then be determined from such nucleotide sequence. The amino acid sequence of the protein encoded by a particular clone can also be determined by expression of the clone in a suitable host cell, collecting the protein and determining its sequence. For each disclosed protein applicants have identified what they have

determined to be the reading frame best identifiable with sequence information available at the time of filing.

As used herein a "secreted" protein is one which, when expressed in a suitable host cell, is transported across or through a membrane, including transport as a result of signal sequences in its amino acid sequence. "Secreted" proteins include without limitation proteins secreted wholly (e.g., soluble proteins) or partially (e.g., receptors) from the cell in which they are expressed. "Secreted" proteins also include without limitation proteins which are transported across the membrane of the endoplasmic reticulum.

## 10 <u>Clone "vb11 1"</u>

15

20

25

A polynucleotide of the present invention has been identified as clone "vb11\_1". vb11\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vb11\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vb11\_1 protein").

The nucleotide sequence of vb11\_1 as presently determined is reported in SEQ ID NO:1, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vb11\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:2. Another potential vb11\_1 reading frame and predicted amino acid sequence that could be encoded by basepairs 84 to 236 of SEQ ID NO:1 is reported in SEQ ID NO:121. Amino acids 13 to 25 of SEQ ID NO:121 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 26 of SEQ ID NO:121. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the protein of SEQ ID NO:121.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vb11\_1 should be approximately 1751 bp.

The nucleotide sequence disclosed herein for vb11\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vb11\_1 demonstrated at least some similarity with sequences identified as N94870 (yy63b05.r1 Homo sapiens cDNA clone 278193 5'). Based upon sequence similarity, vb11\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane

domain within the vb11\_1 protein sequence centered around amino acid 27 of SEQ ID NO:2.

#### Clone "vb12 1"

5

10

15

20

25

30

A polynucleotide of the present invention has been identified as clone "vb12\_1". vb12\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vb12\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vb12\_1 protein").

The nucleotide sequence of vb12\_1 as presently determined is reported in SEQ ID NO:3, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vb12\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:4. Amino acids 34 to 46 of SEQ ID NO:4 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 47. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vb12\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vb12\_1 should be approximately 2289 bp.

The nucleotide sequence disclosed herein for vb12\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vb12\_1 demonstrated at least some similarity with sequences identified as AA426009 (zw49e11.s1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 773420 3', mRNA sequence). Based upon sequence similarity, vb12\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts three additional potential transmembrane domains within the vb12\_1 protein sequence, centered around amino acids 11, 60, and 104 of SEQ ID NO:4, respectively. The nucleotide sequence of vb12\_1 indicates that it may contain a THE1B repeat sequence.

vb12\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 17 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "vb14 1"

10

15

20

25

A polynucleotide of the present invention has been identified as clone "vb14\_1". vb14\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vb14\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vb14\_1 protein").

The nucleotide sequence of vb14\_1 as presently determined is reported in SEQ ID NO:5, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vb14\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:6. Amino acids 79 to 91 of SEQ ID NO:6 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 92. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vb14\_1 protein. Another potential vb14\_1 reading frame and predicted amino acid sequence that could be encoded by basepairs 182 to 484 of SEQ ID NO:5 is reported in SEQ ID NO:122.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vb14\_1 should be approximately 2377 bp.

The nucleotide sequence disclosed herein for vb14\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vb14\_1 demonstrated at least some similarity with sequences identified as AF007149 (Homo sapiens clone 23568, 23621, 23795, 23873 and 23874 mRNA sequences), AF070612 (Homo sapiens clone 24771 mRNA sequence), T23635 (Human gene signature HUMGS05495; standard; cDNA to mRNA), and W02197 (za57e04.r1 Soares fetal liver spleen 1NFLS Homo sapiens cDNA clone 296670 5', mRNA sequence). Based upon sequence similarity, vb14\_1 proteins and each similar protein or peptide may share at least some activity.

# 30 <u>Clone "ve11\_1"</u>

A polynucleotide of the present invention has been identified as clone "vell\_1". vell\_1 was isolated from a human adult brain (Alzheimer's hippocampus level 7) cDNA library and was identified as encoding a secreted or transmembrane protein on the basis

of computer analysis of the amino acid sequence of the encoded protein. vell\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vell\_1 protein").

The nucleotide sequence of ve11\_1 as presently determined is reported in SEQ ID NO:7, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ve11\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:8. Amino acids 1 to 9 of SEQ ID NO:8 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 10. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the ve11\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ve11\_1 should be approximately 984 bp.

The nucleotide sequence disclosed herein for ve11\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ve11\_1 demonstrated at least some similarity with sequences identified as F22745 (H.sapiens EST sequence (LLA5/C09) from skeletal muscle, mRNA sequence) and Q60824 (Human brain Expressed Sequence Tag EST00928; standard; DNA). Based upon sequence similarity, ve11\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the ve11\_1 protein sequence centered around amino acid 35 of SEQ ID NO:8.

#### Clone "vf2 1"

10

15

25

30

A polynucleotide of the present invention has been identified as clone "vf2\_1". vf2\_1 was isolated from a human adult heart cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vf2\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vf2\_1 protein").

The nucleotide sequence of vf2\_1 as presently determined is reported in SEQ ID NO:9, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vf2\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:10. Amino acids 20 to 32

of SEQ ID NO:10 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 33. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vf2\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vf2\_1 should be approximately 1162 bp.

The nucleotide sequence disclosed herein for vf2\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vf2\_1 demonstrated at least some similarity with sequences identified as AA605037 (no68h10.s1 NCI\_CGAP\_AA1 Homo sapiens cDNA clone IMAGE:1112035 similar to contains Alu repetitive element; contains element THR repetitive element; mRNA sequence). Based upon sequence similarity, vf2\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two potential transmembrane domains within the vf2\_1 protein sequence, one centered around amino acid 30 and another around amino acid 70 of SEQ ID NO:10. The nucleotide sequence of vf2\_1 indicates that it may contain an Alu repetitive element.

### 20 <u>Clone "vg2 1"</u>

5

10

15

25

30

A polynucleotide of the present invention has been identified as clone "vg2\_1". vg2\_1 was isolated from a human adult brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vg2\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vg2\_1 protein").

The nucleotide sequence of vg2\_1 as presently determined is reported in SEQ ID NO:11, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vg2\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:12. Amino acids 34 to 46 of SEQ ID NO:12 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 47. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should

the predicted leader/signal sequence not be separated from the remainder of the  $vg2_1$  protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vg2\_1 should be approximately 1993 bp.

5

10

15

20

25

30

The nucleotide sequence disclosed herein for vg2\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vg2\_1 demonstrated at least some similarity with sequences identified as AA830272 (oc45g11.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA clone IMAGE 1352708 3' similar to TR Q92853 Q92853 HU-K4; mRNA sequence) and D31740 (Homo sapiens DNA, CpG island). The predicted amino acid sequence disclosed herein for vg2\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vg2\_1 protein demonstrated at least some similarity to sequences identified as AF026124 (schwannoma-associated protein [Mus musculus]) and U60644 (HU-K4 [Homo sapiens]). Based upon sequence similarity, vg2\_1 proteins and each similar protein or peptide may share at least some activity. Profile hidden markov model analysis (Eddy, S. R., 1996, Curr. Opin. Struct. Biol. 6(3): 361-365; incorporated by reference herein) of the predicted vg2\_1 protein revealed two phospholipase D active sites (amino acid residues 209 to 236 and 423 to 449 of SEQ ID NO:12). Phospholipase D (PLD) genes are members of a superfamily that is defined by several highly conserved motifs. In mammals, it has been proposed that phospholipase D plays a role in membrane vesicular trafficking and in signal transduction. Using site-directed mutagenesis, twenty-five point mutants have been made in human PLD1 (hPLD1) and then characterized (Sung et al., 1997, EMBO J. 16(15): 4519-4530; which is incorporated by reference herein). Sung et al. found that a motif (HxKxxxxD; see for example amino acids 214-221 of SEQ ID NO:12) and a serine/threonine conserved in all members of the PLD superfamily are critical for PLD biochemical activity, suggesting a possible catalytic mechanism. The vg2\_1 clone appears to encode a membrane protein that may be a phospholipase related to the phospholipase D family. The TopPredII computer program predicts four potential transmembrane domains within the vg2\_1 protein sequence, centered around amino acids 40, 305, 330, and 455 of SEQ ID NO:12, respectively.

### Clone "vj1 1"

10

15

A polynucleotide of the present invention has been identified as clone "vj1\_1". vj1\_1 was isolated from a human fetal brain cDNA library (enriched for G-protein-coupled receptors) and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vj1\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vj1\_1 protein").

The nucleotide sequence of vj1\_1 as presently determined is reported in SEQ ID NO:13. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vj1\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:14. Amino acids 1 to 12 of SEQ ID NO:14 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 13. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vj1\_1 protein. Another potential vj1\_1 reading frame and predicted amino acid sequence that could be encoded by basepairs 1795 to 2064 of SEQ ID NO:13 is reported in SEQ ID NO:123.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vj1\_1 should be approximately 2895 bp.

The nucleotide sequence disclosed herein for vj1\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vj1\_1 demonstrated at least some similarity with sequences identified as AA410352 (zv11f01.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 753337 5', mRNA sequence). Based upon sequence similarity, vj1\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the vj1\_1 protein sequence centered around amino acid 70 of SEQ ID NO:14. The nucleotide sequence of vj1\_1 indicates that it may contain repetitive elements.

# 30 <u>Clone "vl1\_1"</u>

A polynucleotide of the present invention has been identified as clone "vl1\_1". vl1\_1 was isolated from a human fetal cartilage cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the

amino acid sequence of the encoded protein. vl1\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vl1\_1 protein").

The nucleotide sequence of vl1\_1 as presently determined is reported in SEQ ID NO:15, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vl1\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:16. Amino acids 187 to 199 of SEQ ID NO:16 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 200. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vl1\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vl1\_1 should be approximately 1936 bp.

10

30

The nucleotide sequence disclosed herein for vl1\_1 was searched against the 15 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vl1\_1 demonstrated at least some similarity with sequences identified as AA464362 (zx81b12.r1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 810143 5', mRNA sequence), M90089 (Mouse inositol 1,4,5-triphosphate receptor mRNA sequence), and T21689 (Human gene signature HUMGS03131; standard; cDNA 20 to mRNA). The predicted amino acid sequence disclosed herein for vl1\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vl1\_1 protein demonstrated at least some similarity to the sequence identified as U80846 (partial CDS [Caenorhabditis elegans]). Based upon sequence similarity, vl1\_1 proteins and each similar protein or peptide may share at least 25 The TopPredII computer program predicts two additional potential some activity. transmembrane domains within the vl1\_1 protein sequence, one centered around amino acid 192 and another around amino acid 234 of SEQ ID NO:16.

vll\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 37 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

### Clone "vk2 1"

10

15

20

25

A polynucleotide of the present invention has been identified as clone "vk2\_1". vk2\_1 was isolated from a human adult brain cDNA library (enriched for G-protein-coupled receptors) and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vk2\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vk2\_1 protein").

The nucleotide sequence of vk2\_1 as presently determined is reported in SEQ ID NO:17, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vk2\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:18. Amino acids 10 to 22 of SEQ ID NO:18 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 23. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vk2\_1 protein. Basepairs 416 to 418 of SEQ ID NO:17 may represent the site of an alternatively spliced exon that is not present in clone vk2\_1.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vk2\_1 should be approximately 1284 bp.

The nucleotide sequence disclosed herein for vk2\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vk2\_1 demonstrated at least some similarity with sequences identified as AA152101 (zl49f09.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 505289 3', mRNA sequence) and Q78696 (Sequence encoding therapeutic polypeptide from glioblastoma cell line; standard; cDNA to mRNA). The predicted amino acid sequence disclosed herein for vk2\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vk2\_1 protein demonstrated at least some similarity to the sequence identified as R66278 (Therapeutic polypeptide from glioblastoma cell line). Based upon sequence similarity, vk2\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two additional potential transmembrane domains within the vk2\_1 protein sequence, one centered around amino acid 61 and another around amino acid 97 of SEQ ID NO:18.

#### Clone "vb21 1"

10

15

20

25

A polynucleotide of the present invention has been identified as clone "vb21\_1". vb21\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vb21\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vb21\_1 protein").

The nucleotide sequence of vb21\_1 as presently determined is reported in SEQ ID NO:19, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vb21\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:20. Amino acids 296 to 308 of SEQ ID NO:20 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 309. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vb21\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vb21\_1 should be approximately 4159 bp.

The nucleotide sequence disclosed herein for vb21\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vb21\_1 demonstrated at least some similarity with sequences identified as AA026150 (zj99c10.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 469170 3', mRNA sequence), T72108 (Human semaphorin Z gene; standard; cDNA to mRNA), U52840 (Human semaphorin F homolog), X97817 (M. musculus mRNA for semaphorin F), and X97818 (M. musculus mRNA for semaphorin G). The predicted amino acid sequence disclosed herein for vb21\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vb21\_1 protein demonstrated at least some similarity to sequences identified as W19857 (Human semaphorin Z) and X97818 (samaphorin G [Mus musculus]). Semaphorins are important membrane proteins involved in axonal guidance in the embryonic stage, and may also have a role in nerve regeneration after injury. Based upon sequence similarity, vb21\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts four additional potential transmembrane domains within the vb21\_1 protein sequence, centered around amino acids 237, 523, 769, and 895 of SEQ ID NO:20, respectively.

#### Clone "vc35 1"

10

15

20

25

A polynucleotide of the present invention has been identified as clone "vc35\_1". vc35\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc35\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc35\_1 protein").

The nucleotide sequence of vc35\_1 as presently determined is reported in SEQ ID NO:21, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc35\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:22. Amino acids 38 to 50 of SEQ ID NO:22 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 51. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc35\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc35\_1 should be approximately 3042 bp.

The nucleotide sequence disclosed herein for vc35\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc35\_1 demonstrated at least some similarity with sequences identified as AA532364 (nj12a08.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA clone IMAGE:986102, mRNA sequence), AF029343 (human protocadherin 68), and T22263 (Human gene signature HUMGS03835; standard; cDNA to mRNA). The predicted amino acid sequence disclosed herein for vc35\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vc35\_1 protein demonstrated at least some similarity to sequences identified as Y08715 (protocadherin-4 [Mus musculus]). Based upon sequence similarity, vc35\_1 proteins and each similar protein or peptide may share at least some activity.

# 30 <u>Clone "vc36\_1"</u>

A polynucleotide of the present invention has been identified as clone "vc36\_1". vc36\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the

amino acid sequence of the encoded protein. vc36\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc36\_1 protein").

The nucleotide sequence of vc36\_1 as presently determined is reported in SEQ ID NO:23, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc36\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:24. Amino acids 24 to 36 of SEQ ID NO:24 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 37. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc36\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc36\_1 should be approximately 1395 bp.

The nucleotide sequence disclosed herein for vc36\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc36\_1 demonstrated at least some similarity with sequences identified as AA259070 (zs33c04.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA clone IMAGE 686982 5', mRNA sequence) and W67508 (zd40f11.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 343149 3', mRNA sequence). Based upon sequence similarity, vc36\_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of vc36\_1 indicates that it may contain repetitive elements.

#### Clone "vc38\_1"

10

15

20

25

30

A polynucleotide of the present invention has been identified as clone "vc38\_1". vc38\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc38\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc38\_1 protein").

The nucleotide sequence of vc38\_1 as presently determined is reported in SEQ ID NO:25, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc38\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:26.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc38\_1 should be approximately 2468 bp.

The nucleotide sequence disclosed herein for vc38\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc38\_1 demonstrated at least some similarity with sequences identified as AF037400 (neuropeptide Y/peptide YY receptor Ya [Danio rerio]). Motifs analysis and profile hidden markov model analysis of the predicted vc38\_1 protein both reveal the presence of the G-protein-coupled receptor signature. G-protein-coupled receptors (also called R7G) are an extensive group of hormones, neurotransmitters, odorants, and light receptors which transduce extracellular signals by interaction with guanine nucleotide-binding (G) proteins. Most G-protein-coupled receptors lack a signal peptide, as does the predicted vc38\_1 protein. Based upon sequence similarity, vc38\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts seven potential transmembrane domains within the vc38\_1 protein sequence, centered around amino acids 60, 90, 130, 170, 225, 280, and 318 of SEQ ID NO:26, respectively.

vc38\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 71 kDa was detected in conditioned medium using SDS polyacrylamide gel electrophoresis.

#### Clone "vc39 1"

10

15

20

25

30

A polynucleotide of the present invention has been identified as clone "vc39\_1". vc39\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc39\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc39\_1 protein").

The nucleotide sequence of vc39\_1 as presently determined is reported in SEQ ID NO:27, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc39\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:28. Amino acids 2 to 14 of SEQ ID NO:28 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 15. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc39\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc39\_1 should be approximately 2048 bp.

The nucleotide sequence disclosed herein for vc39\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and 5 FASTA search protocols. vc39\_1 demonstrated at least some similarity with sequences identified as AA631722 (np79d04.s1 NCI\_CGAP\_Pr2 Homo sapiens cDNA clone IMAGE:1132519 similar to gb:M21121 T-CELL SPECIFIC RANTES PROTEIN PRECURSOR (HUMAN); contains Alu repetitive element; mRNA sequence). Based upon sequence similarity, vc39\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the vc39\_1 protein sequence centered around amino acid 40 of SEQ ID NO:28. The nucleotide sequence of vc39\_1 indicates that it may contain an Alu/SVA repetitive element.

#### 15 Clone "vc40 1"

10

20

25

A polynucleotide of the present invention has been identified as clone "vc40\_1". vc40\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc40\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc40\_1 protein").

The nucleotide sequence of vc40\_1 as presently determined is reported in SEQ ID NO:29, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc40\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:30. Amino acids 19 to 31 of SEQ ID NO:30 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 32. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc40\_1 protein.

30 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc40\_1 should be approximately 2297 bp.

The nucleotide sequence disclosed herein for vc40\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc40\_1 demonstrated at least some similarity with sequences

identified as AA143014 (zl48g04.r1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 505206 5', mRNA sequence) and T20006 (Human gene signature HUMGS01143; standard; cDNA to mRNA). Based upon sequence similarity, vc40\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts three additional potential transmembrane domains within the vc40\_1 protein sequence, centered around amino acids 101, 136, and 182 of SEQ ID NO:30, respectively.

# Clone "vc46 1"

15

20

25

30

A polynucleotide of the present invention has been identified as clone "vc46\_1".

vc46\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc46\_1 is a full-length clone, including the

entire coding sequence of a secreted protein (also referred to herein as "vc46\_1 protein").

The nucleotide sequence of vc46\_1 as presently determined is reported in SEQ ID NO:31, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc46\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:32. Amino acids 10 to 22 of SEQ ID NO:32 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 23. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc46\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc46\_1 should be approximately 2938 bp.

The nucleotide sequence disclosed herein for vc46\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc46\_1 demonstrated at least some similarity with sequences identified as AA029404 (ze94e06.r1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 366658 5', mRNA sequence) and AQ071029 (human genomic fragment). Based upon sequence similarity, vc46\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two additional potential transmembrane domains within the vc46\_1 protein sequence, one centered around amino acid 70 and another around amino acid 130 of SEQ ID NO:32.

vc46\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 19 kDa was detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "vc49 1"

5

10

15

20

25

30

A polynucleotide of the present invention has been identified as clone "vc49\_1". vc49\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc49\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc49\_1 protein").

The nucleotide sequence of vc49\_1 as presently determined is reported in SEQ ID NO:33, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc49\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:34. Amino acids 14 to 26 of SEQ ID NO:34 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 27. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc49\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc49\_1 should be approximately 3471 bp.

The nucleotide sequence disclosed herein for vc49\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc49\_1 demonstrated at least some similarity with sequences identified as AI075929 (ov46h11.x1 Soares\_testis\_NHT Homo sapiens cDNA clone IMAGE 1640421 3' similar to TR Q63418 Q63418 PROTOCADHERIN-3; mRNA sequence), I79964 (Sequence 109 from patent US 5708143), and T03572 (Human protocadherin pc3 coding sequence; standard; cDNA). The predicted amino acid sequence disclosed herein for vc49\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vc49\_1 protein demonstrated at least some similarity to sequences identified as L43592 (protocadherin-3 [Rattus norvegicus]) and R86865 (Human protocadherin pc3). Based upon sequence similarity, vc49\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two potential transmembrane domains within the vc49\_1

protein sequence, one definite transmembrane domain centered around amino acid 700 and another possible transmembrane domain centered around amino acid 260 of SEQ ID NO:34. Profile hidden markov model and motifs analyses of the predicted vc49\_1 protein sequence have revealed it to contain five cadherin extracellular repeated domain signatures at amino acids 142 to 242, 251 to 347, 356 to 451, 460 to 561, and 576 to 671 of SEQ ID NO:34. Cadherins are a family of animal glyco-proteins responsible for calcium-dependent cell-cell adhesion. Cadherins preferentially interact with themselves in a homophilic manner in connecting cells; thus acting as both receptor and ligand. Structurally, cadherins are built of the following domains: a signal sequence, followed by a propeptide of about 130 residues, then an extracellular domain of around 600 residues, then a transmembrane region, and finally a C-terminal cytoplasmic domain of about 150 residues. The predicted vc49\_1 protein sequence almost exactly follows this structure (its cytoplasmic domain being approximately 100 amino acids). Clearly, vc49\_1 protein appears to represent a novel member of the cadherin superfamily.

15

20

25

30

10

#### Clone "vc50 1"

A polynucleotide of the present invention has been identified as clone "vc50\_1". vc50\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc50\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc50\_1 protein").

The nucleotide sequence of vc50\_1 as presently determined is reported in SEQ ID NO:35, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc50\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:36. Amino acids 20 to 32 of SEQ ID NO:36 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 33. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc50\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc50\_1 should be approximately 3819 bp.

The nucleotide sequence disclosed herein for vc50\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and

FASTA search protocols. vc50\_1 demonstrated at least some similarity with sequences identified as AA193122 (zr39d05.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 665769 5', mRNA sequence), T26031 (Human gene signature HUMGS08267; standard; cDNA to mRNA), Z31718 (H.sapiens gene for myelin protein zero), and Z99943 (Human DNA sequence from PAC 313L4 on chromosome 1q24). The predicted amino acid sequence disclosed herein for vc50\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vc50\_1 protein demonstrated at least some similarity to the sequence identified as K03242 (rat P0 myelin prepeptide), L24893 (myelin protein zero [Homo sapiens]), and M62860 (mouse peripheral myelin protein). Based upon sequence similarity, vc50\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the vc50\_1 protein sequence centered around amino acid 181 of SEQ ID NO:36.

vc50\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 26 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

#### <u>Clone "vc51\_1"</u>

10

15

20

25

A polynucleotide of the present invention has been identified as clone "vc51\_1". vc51\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc51\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc51\_1 protein").

The nucleotide sequence of vc51\_1 as presently determined is reported in SEQ ID NO:37, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc51\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:38. Amino acids 12 to 24 of SEQ ID NO:38 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 25. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc51\_1 protein. If the "G" residue at position 388 of SEQ ID NO:37 were deleted, two alternative potential vc51\_1 reading frames and predicted amino acid sequences that could be

encoded by basepairs 333 to 1310 of SEQ ID NO:37 and by basepairs 139 to 522 of SEQ ID NO:37 are reported in SEQ ID NO:124 and SEQ ID NO:125, respectively.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc51\_1 should be approximately 1992 bp.

The nucleotide sequence disclosed herein for vc51\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc51\_1 demonstrated at least some similarity with sequences identified as T21514 (Human gene signature HUMGS02887; standard; cDNA to mRNA) and W52782 (zd13h06.r1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 340571 10 5', mRNA sequence). The predicted amino acid sequence disclosed herein for vc51\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vc51\_1 protein demonstrated at least some similarity to sequences identified as U90716 (human cell surface protein HCAR), Y07593 (coxsackie and adenovirus receptor protein [Homo sapiens]), Y10320 (mouse coxsackie and adenovirus receptor homolog), and W14146 (Human A33 antigen). Based upon sequence similarity, vc51\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts four additional potential transmembrane domains within the vc51\_1 protein sequence centered around amino acids 17, 216, 260, and 373 of SEQ ID NO:38, respectively.

20

25

15

5

#### Clone "vc52 1"

A polynucleotide of the present invention has been identified as clone "vc52\_1". vc52\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc52\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc52\_1 protein").

The nucleotide sequence of vc52\_1 as presently determined is reported in SEQ ID NO:39, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc52\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:40. Amino acids 19 to 31 of SEQ ID NO:40 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 32. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should

the predicted leader/signal sequence not be separated from the remainder of the vc52\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc52\_1 should be approximately 2018 bp.

The nucleotide sequence disclosed herein for vc52\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc52\_1 demonstrated at least some similarity with sequences identified as AA075627 (zm89a01.s1 Stratagene ovarian cancer (#937219) Homo sapiens cDNA clone 545064 3', mRNA sequence) and T24879 (Human gene signature HUMGS06985; standard; cDNA to mRNA). The predicted amino acid sequence disclosed herein for vc52\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vc52\_1 protein demonstrated at least some similarity to sequences identified as AL021890 (putative protein [Arabidopsis thaliana]), L47993 (ORF YJR072c [Saccharomyces cerevisiae]), and U10402 (undefined protein [Caenorhabditis elegans]). Based upon sequence similarity, vc52\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the vc52\_1 protein sequence centered around amino acid 145 of SEQ ID NO:40.

vc52\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 44 kDa was detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

# Clone "vc33 1"

5

10

15

20

25

A polynucleotide of the present invention has been identified as clone "vc33\_1". vc33\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc33\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc33\_1 protein").

The nucleotide sequence of vc33\_1 as presently determined is reported in SEQ ID NO:41, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc33\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:42. Amino acids 99 to 111 of SEQ ID NO:42 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 112. Due to the hydrophobic nature of the

predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc33\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc33\_1 should be approximately 2877 bp.

The nucleotide sequence disclosed herein for vc33\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc33\_1 demonstrated at least some similarity with sequences identified as AA846599 (aj97g02.s1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone IMAGE:1404434 3' similar to gb:M95549 SODIUM/GLUCOSE COTRANSPORTER-LIKE (HUMAN); mRNA sequence), M95549 (Homo sapiens sodium/glucose cotransporter-like protein mRNA, complete cds), and Q89779 (Cotransporter protein SNST1 cDNA; standard; cDNA). The predicted amino acid sequence disclosed herein for vc33\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vc33\_1 protein demonstrated at least some similarity to sequences identified as M95549 (sodium/glucose cotransporter-like protein [Homo sapiens]) and R73593 (Cotransporter protein SNST1). Based upon sequence similarity, vc33\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts three additional potential transmembrane domains within the vc33\_1 protein sequence, centered around amino acids 186, 260, and 324 of SEQ ID NO:42, respectively.

vc33\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 45 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "vc34 1"

10

15

20

25

A polynucleotide of the present invention has been identified as clone "vc34\_1". vc34\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc34\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc34\_1 protein").

The nucleotide sequence of vc34\_1 as presently determined is reported in SEQ ID NO:43, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc34\_1 protein corresponding

to the foregoing nucleotide sequence is reported in SEQ ID NO:44. Amino acids 4 to 16 of SEQ ID NO:44 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 17. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc34\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc34\_1 should be approximately 3062 bp.

The nucleotide sequence disclosed herein for vc34\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc34\_1 demonstrated at least some similarity with sequences identified as AA927558 (om71e04.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA clone IMAGE 1552638 3', mRNA sequence) and U79281 (Human clone 23588 mRNA sequence). Based upon sequence similarity, vc34\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two additional potential transmembrane domains within the vc34\_1 protein sequence, one centered around amino acid 251 and another around amino acid 283 of SEQ ID NO:44.

vc34\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 72 kDa was detected in conditioned medium using SDS polyacrylamide gel electrophoresis.

## Clone "vc47 1"

10

15

20

25

A polynucleotide of the present invention has been identified as clone "vc47\_1". vc47\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc47\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc47\_1 protein").

The nucleotide sequence of vc47\_1 as presently determined is reported in SEQ ID NO:45, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc47\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:46. Amino acids 93 to 105 of SEQ ID NO:46 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 106. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should

the predicted leader/signal sequence not be separated from the remainder of the vc47\_1 protein.

Another potential vc47\_1 reading frame and predicted amino acid sequence that could be encoded by basepairs 1047 to 1322 of SEQ ID NO:45 is reported in SEQ ID NO:126. Amino acids 11 to 23 of SEQ ID NO:126 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24. Due to the hydrophobic nature of this predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the protein of SEQ ID NO:126.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc47\_1 should be approximately 3676 bp.

The nucleotide sequence disclosed herein for vc47\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc47\_1 demonstrated at least some similarity with sequences identified as AA339320 (EST44392 Fetal brain I Homo sapiens cDNA 5' end, mRNA sequence) and R02462 (ye82h04.r1 Homo sapiens cDNA clone 124279 5'). Based upon sequence similarity, vc47\_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of vc47\_1 indicates that it may contain one or more of the following repetitive elements: Alu, L1MB7.

20

25

15

10

# Clone "vc54\_1"

A polynucleotide of the present invention has been identified as clone "vc54\_1". vc54\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc54\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc54\_1 protein").

The nucleotide sequence of vc54\_1 as presently determined is reported in SEQ ID NO:47, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc54\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:48. Amino acids 33 to 45 of SEQ ID NO:48 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 46. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should

the predicted leader/signal sequence not be separated from the remainder of the vc54\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc54\_1 should be approximately 2083 bp.

The nucleotide sequence disclosed herein for vc54\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc54\_1 demonstrated at least some similarity with sequences identified as AF007152 (Homo sapiens clone 23649 and 23755 unknown mRNA, partial cds), Q76901 (Human genome fragment (Preferred); standard; DNA), and T46905 (EST014 BL29 Burkitt's lymphoma, Pascalis Sideras Homo sapiens cDNA clone BL29-14 5', mRNA sequence). The predicted amino acid sequence disclosed herein for vc54\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vc54\_1 protein demonstrated at least some similarity to the sequence identified as AF007152 (unknown [Homo sapiens]). Based upon sequence similarity, vc54\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two additional potential transmembrane domains within the vc54\_1 protein sequence, one centered around amino acid 220 and another around amino acid 247 of SEQ ID NO:48.

vc54\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 44 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "vc57 1"

5

10

15

20

25

30

A polynucleotide of the present invention has been identified as clone "vc57\_1". vc57\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc57\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc57\_1 protein").

The nucleotide sequence of vc57\_1 as presently determined is reported in SEQ ID NO:49, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc57\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:50. Amino acids 15 to 27 of SEQ ID NO:50 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 28. Due to the hydrophobic nature of the

predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc57\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc57\_1 should be approximately 2564 bp.

The nucleotide sequence disclosed herein for vc57\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc57\_1 demonstrated at least some similarity with sequences identified as AA156231 (zl50a11.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 505340 3', mRNA sequence). The predicted amino acid sequence disclosed herein for vc57\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vc57\_1 protein demonstrated at least some similarity to the sequence identified as U41635 (OS-9 precursor [Homo sapiens]). Based upon sequence similarity, vc57\_1 proteins and each similar protein or peptide may share at least some activity.

vc57\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 51 kDa was detected in conditioned medium using SDS polyacrylamide gel electrophoresis.

# 20 <u>Clone "ve13 1"</u>

5

10

15

25

30

A polynucleotide of the present invention has been identified as clone "ve13\_1". ve13\_1 was isolated from a human adult brain (Alzheimer's hippocampus level 7) cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ve13\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ve13\_1 protein").

The nucleotide sequence of ve13\_1 as presently determined is reported in SEQ ID NO:51, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ve13\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:52. Amino acids 551 to 563 of SEQ ID NO:52 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 564. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should

the predicted leader/signal sequence not be separated from the remainder of the ve13\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ve13\_1 should be approximately 3046 bp.

The nucleotide sequence disclosed herein for ve13\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ve13\_1 demonstrated at least some similarity with sequences identified as AA587395 (nn82h06.s1 NCI\_CGAP\_Co9 Homo sapiens cDNA clone IMAGE:1090427 similar to contains element THR repetitive element; mRNA sequence) and Q76778 (Human genome fragment (Preferred); standard; DNA). The predicted amino acid sequence disclosed herein for ve13\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted ve13\_1 protein demonstrated at least some similarity to the sequence identified as U50828 (sel-1 gene product [Caenorhabditis elegans]). Based upon sequence similarity, ve13\_1 proteins and each similar protein or peptide may share at least some activity.

#### Clone "ve16 1"

5

10

15

20

25

30

A polynucleotide of the present invention has been identified as clone "ve16\_1". ve16\_1 was isolated from a human adult brain (Alzheimer's hippocampus level 7) cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ve16\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ve16\_1 protein").

The nucleotide sequence of ve16\_1 as presently determined is reported in SEQ ID NO:53, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ve16\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:54. Amino acids 14 to 26 of SEQ ID NO:54 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 27. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the ve16\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ve16\_1 should be approximately 2033 bp.

The nucleotide sequence disclosed herein for ve16\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No hits were found in the databases. The nucleotide sequence of ve16\_1 indicates that it may contain one or more of the following repetitive elements: Alu, MER.

## Clone "vf3 1"

5

10

15

20

25

30

A polynucleotide of the present invention has been identified as clone "vf3\_1". vf3\_1 was isolated from a human adult heart cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vf3\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vf3\_1 protein").

The nucleotide sequence of vf3\_1 as presently determined is reported in SEQ ID NO:55, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vf3\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:56. Amino acids 8 to 20 of SEQ ID NO:56 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 21. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vf3\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vf3\_1 should be approximately 2987 bp.

The nucleotide sequence disclosed herein for vf3\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vf3\_1 demonstrated at least some similarity with sequences identified as Z78394 (H.sapiens mRNA, expressed sequence tag ICRFp507K11187 (5'), mRNA sequence). The predicted amino acid sequence disclosed herein for vf3\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vf3\_1 protein demonstrated at least some similarity to the sequence identified as U41558 (K02B2.3 gene product [Caenorhabditis elegans]). Based upon sequence similarity, vf3\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two

additional potential transmembrane domains within the vf3\_1 protein sequence, one centered around amino acid 242 and another around amino acid 275 of SEQ ID NO:56.

vf3\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 39 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

# Clone "vi2 1"

10

15

20

25

30

A polynucleotide of the present invention has been identified as clone "vj2\_1". vj2\_1 was isolated from a human fetal brain (whole brain, enriched for G-protein-coupled receptors) cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vj2\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vj2\_1 protein").

The nucleotide sequence of vj2\_1 as presently determined is reported in SEQ ID NO:57, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vj2\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:58. Amino acids 59 to 71 of SEQ ID NO:58 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 72. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vj2\_1 protein.

Another potential vj2\_1 reading frame and predicted amino acid sequence that could be encoded by basepairs 146 to 400 of SEQ ID NO:57 is reported in SEQ ID NO:127. The TopPredII computer program predicts two potential transmembrane domains within the amino acid sequence of SEQ ID NO:127.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vj2\_1 should be approximately 1762 bp.

The nucleotide sequence disclosed herein for vj2\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vj2\_1 demonstrated at least some similarity with sequences identified as N36445 (yx83c04.r1 Homo sapiens cDNA clone 268326 5'). Based upon sequence similarity, vj2\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts three potential transmembrane

domains within the vj2\_1 protein sequence, centered around amino acids 30, 67, and 90 of SEQ ID NO:58, respectively. The nucleotide sequence of vj2\_1 indicates that it may contain one or more repetitive elements.

# 5 <u>Clone "vp7 1"</u>

10

15

20

25

30

A polynucleotide of the present invention has been identified as clone "vp7\_1". vp7\_1 was isolated from a human adult prostate cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vp7\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vp7\_1 protein").

The nucleotide sequence of vp7\_1 as presently determined is reported in SEQ ID NO:59, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vp7\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:60. Amino acids 6 to 18 of SEQ ID NO:60 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 19. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vp7\_1 protein. Another potential vp7\_1 reading frame and predicted amino acid sequence that could be encoded by basepairs 2071 to 2430 of SEQ ID NO:59 is reported in SEQ ID NO:128.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vp7\_1 should be approximately 2638 bp.

The nucleotide sequence disclosed herein for vp7\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vp7\_1 demonstrated at least some similarity with sequences identified as N49433 (yv21e12.r1 Homo sapiens cDNA clone 243406 5') and Q63862 (AP2 sequence obtained by PCR for tumour specific DNA; standard; cDNA). Based upon sequence similarity, vp7\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the vp7\_1 protein sequence centered around amino acid 75 of SEQ ID NO:60. The nucleotide sequence of vp7\_1 indicates that it may contain one or more Alu repeat sequences.

# Clone "vp8 1"

5

10

15

25

A polynucleotide of the present invention has been identified as clone "vp8\_1". vp8\_1 was isolated from a human adult prostate cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vp8\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vp8\_1 protein").

The nucleotide sequence of vp8\_1 as presently determined is reported in SEQ ID NO:61, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vp8\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:62. Amino acids 20 to 32 of SEQ ID NO:62 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 33. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vp8\_1 protein. If two insertions of "C" residues were made in the nucleotide sequence of SEQ ID NO:61, one after the "A" at position 380 and another after the "G" at position 382, the resulting nucleotide sequence would be predicted to encode the amino acid sequence reported in SEQ ID NO:129.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vp8\_1 should be approximately 1513 bp.

The nucleotide sequence disclosed herein for vp8\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vp8\_1 demonstrated at least some similarity with sequences identified as AA284421 (zs59c10.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA clone IMAGE 701778 5' similar to contains Alu repetitive element; mRNA sequence) and AC002086 (Human PAC clone DJ525N14 from Xq23, complete sequence). Based upon sequence similarity, vp8\_1 proteins and each similar protein or peptide may share at least some activity. Profile hidden markov model analysis reveals the presence of an SH2 domain in the predicted vp8\_1 protein (SEQ ID NO:62). SH2 domains function as regulatory modulators of intra-cellular signalling cascades by interacting with high affinity to phosphotyrosine-containing target peptides in a sequence-specific and strictly phosphorylation-dependent manner. The nucleotide sequence of vp8\_1 indicates that it may contain one or more Alu repeat sequences.

vp8\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 34 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

# <u>Clone "vb22\_1"</u>

5

10

15

A polynucleotide of the present invention has been identified as clone "vb22\_1". vb22\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vb22\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vb22\_1 protein").

The nucleotide sequence of vb22\_1 as presently determined is reported in SEQ ID NO:63, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vb22\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:64. Another potential vb22\_1 reading frame and predicted amino acid sequence is encoded by basepairs 152 to 1006 of SEQ ID NO:63 and is reported in SEQ ID NO:130.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vb22\_1 should be approximately 4176 bp.

The nucleotide sequence disclosed herein for vb22\_1 was searched against the 20 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vb22\_1 demonstrated at least some similarity with sequences identified as L10335 (Homo sapiens neuroendocrine-specific protein C (NSP) mRNA, complete cds), N21304 (yx53f07.s1 Homo sapiens cDNA clone 265477 3' similar to SP:A60021 A60021 TROPOMYOSIN-RELATED PROTEIN, NEURONAL), and V23695 (Human NSPLP protein A coding sequence; standard; cDNA). The predicted amino acid 25 sequence disclosed herein for vb22\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vb22\_1 protein demonstrated at least some similarity to sequences identified as L10333 (nueroendocrine-specific protein A [Homo sapiens]) and W53947 (Human NSPLP protein 30 A). Based upon sequence similarity, vb22\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two potential transmembrane domains within the vb22\_1 protein sequence, one centered around amino acid 730 and another around amino acid 846 of SEQ ID NO:64. The nucleotide sequence of vb22\_1 appears to contain a short simple nucleotide repeat ("GGA") region.

#### Clone "vc48 1" ·

5

10

15

20

25

A polynucleotide of the present invention has been identified as clone "vc48\_1". vc48\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc48\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc48\_1 protein").

The nucleotide sequence of vc48\_1 as presently determined is reported in SEQ ID NO:65, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vc48\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:66. Amino acids 7 to 19 of SEQ ID NO:66 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 20. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc48\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc48\_1 should be approximately 3096 bp.

The nucleotide sequence disclosed herein for vc48\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc48\_1 demonstrated at least some similarity with sequences identified as AA292779 (zt56c06.s1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 726346 3', mRNA sequence). The predicted amino acid sequence disclosed herein for vc48\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vc48\_1 protein demonstrated at least some similarity to sequences identified as AL031765 (Drosophila genomic product 22E5.z) and Z81058 (F11E6.e [Caenorhabditis elegans]). Based upon sequence similarity, vc48\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts four potential transmembrane domains within the vc48\_1 protein sequence, one centered around amino acid 39 and others around amino acids 69, 107 and 134 of SEQ ID NO:66, respectively. The nucleotide sequence of vc48\_1 appears to contain a simple nucleotide repeat ("AC") and one or more of the following repetitive elements: Alu and MIR.

### Clone "vp3 1"

10

15

20

25

30

A polynucleotide of the present invention has been identified as clone "vp3\_1". vp3\_1 was isolated from a human adult prostate cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vp3\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vp3\_1 protein").

The nucleotide sequence of vp3\_1 as presently determined is reported in SEQ ID NO:67, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vp3\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:68. Amino acids 19 to 31 of SEQ ID NO:68 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 32. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vp3\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vp3\_1 should be approximately 552 bp.

The nucleotide sequence disclosed herein for vp3\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vp3\_1 demonstrated at least some similarity with sequences identified as AA225045 (nc34c06.r1 NCI\_CGAP\_Pr2 Homo sapiens cDNA clone IMAGE 1010026, mRNA sequence), M18157 (Human glandular kallikrein gene, complete cds), and T35868 (Prostate-specific antigen gene partial sequence; standard; DNA). Based upon sequence similarity, vp3\_1 proteins and each similar protein or peptide may share at least some activity.

# Clone "vc61 1"

A polynucleotide of the present invention has been identified as clone "vc61\_1". vc61\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vc61\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vc61\_1 protein").

The nucleotide sequence of vc61\_1 as presently determined is reported in SEQ ID NO:69, and includes a poly(A) tail. What applicants presently believe to be the proper

PCT/US99/19351 WO 00/11015

reading frame and the predicted amino acid sequence of the vc61\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:70. Amino acids 16 to 28 of SEQ ID NO:70 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 29. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vc61\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vc61\_1 should be approximately 3199 bp.

10 The nucleotide sequence disclosed herein for vc61\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vc61\_1 demonstrated at least some similarity with sequences identified as AI028115 (ow51d09.x1 Soares\_parathyroid\_tumor\_NbHPA Homo sapiens cDNA clone IMAGE 1650353 3' similar to gb S67859 TRANSCRIPTION INITIATION FACTOR IIE-ALPHA CHAIN (HUMAN); mRNA), V20913 (Human induced tumour protein cDNA), and Z99129 (Human DNA sequence from clone 425C14 on chromosome 6q22 Contains the HSF2 gene for Heat Shock Factor 2 (Heat Shock Transcription Factor 2, HSTF 2) and an unknown gene similar to the placental protein DIFF33 gene; Contains ESTs, STSs and GSSs, complete sequence). The predicted amino acid sequence disclosed herein for vc61\_1 was searched against the GenPept and GeneSeq amino acid sequence 20 databases using the BLASTX search protocol. The predicted vc61\_1 protein demonstrated at least some similarity to sequences identified as W52812 (Human induced tumour protein) and Z99129 (dJ425C14.2 (Placental protein DIFF33 LIKE) [Homo sapiens]). The deduced vc61\_1 protein has amino acid similarity to human and mouse diff33 protein. Diff33 is a transmembrane protein which is overexpressed in testicular tumors from polyomavirus large T-antigen transgenic mice. Based upon sequence similarity, vc61\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts nine additional potential transmembrane domains within the vc61\_1 protein sequence, centered around amino acids 50, 100, 150, 210, 240, 270, 320, 390, and 430 of SEQ ID NO:70, respectively. The nucleotide sequence of vc61 $_{-1}$ indicates that it may contain an Alu repetitive element.

25

30

## Clone "vp15 1"

10

20

25

30

A polynucleotide of the present invention has been identified as clone "vp15\_1". vp15\_1 was isolated from a human adult prostate cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vp15\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vp15\_1 protein").

The nucleotide sequence of vp15\_1 as presently determined is reported in SEQ ID NO:71, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vp15\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:72. Amino acids 4 to 16 of SEQ ID NO:72 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 17. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vp15\_1 protein. If a "C" residue were inserted between nucleotides 458 and 459 of SEQ ID NO:71, nucleotides 44 to 568 of the resulting nucleotide sequence would encode a protein having an amino acid sequence reported as SEQ ID NO:131.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vp15\_1 should be approximately 2033 bp.

The nucleotide sequence disclosed herein for vp15\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vp15\_1 demonstrated at least some similarity with sequences identified as AI033082 (ow97g04.s1 Soares\_fetal\_liver\_spleen\_1NFLS\_S1 Homo sapiens cDNA clone IMAGE 1654806 3', mRNA sequence) and T21877 (Human gene signature HUMGS03418). The predicted amino acid sequence disclosed herein for vp15\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vp15\_1 protein demonstrated at least some similarity to sequences identified as R45335 (Thrombomodulin analogue Q336N, Q365E) and U94333 (C1qR(p) [Homo sapiens]). The predicted vp15\_1 protein shows some amino acid similarity to multiple thrombomodulin analogues (such as GeneSeq accession number R45335), and shows some end-to-end similarity to GenPept accession number U94333, which is described as a "... human C1q/MBL/SPA receptor that mediates enhanced phagocytosis in vitro" (Nepomuceno et al., 1997, Immunity 6(2): 119-129, which

is incorporated by reference herein). Based upon sequence similarity, vp15\_1 proteins and each similar protein or peptide may share at least some activity.

vp15\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 24 kDa was detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

# Clone "vp17 1"

5

10

15

20

A polynucleotide of the present invention has been identified as clone "vp17\_1". vp17\_1 was isolated from a human adult prostate cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vp17\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vp17\_1 protein").

The nucleotide sequence of vp17\_1 as presently determined is reported in SEQ ID NO:73, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vp17\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:74. Amino acids 10 to 22 of SEQ ID NO:74 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 23. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vp17\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vp17\_1 should be approximately 3150 bp.

The nucleotide sequence disclosed herein for vp17\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vp17\_1 demonstrated at least some similarity with sequences identified as AI056890 (oz03g07.x1 Soares\_fetal\_liver\_spleen\_1NFLS\_S1 Homo sapiens cDNA clone IMAGE 1674300 3', mRNA sequence) and T64815 (Tumour suppressor activated pathway gene TSAP6). Based upon sequence similarity, vp17\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two additional potential transmembrane domains within the vp17\_1 protein sequence, one centered around amino acid 50 and another around amino acid 80 of SEQ ID NO:74.

# Clone "vp19 1"

A polynucleotide of the present invention has been identified as clone "vp19\_1". vp19\_1 was isolated from a human adult prostate cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vp19\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vp19\_1 protein").

The nucleotide sequence of vp19\_1 as presently determined is reported in SEQ ID NO:75, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vp19\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:76.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vp19\_1 should be approximately 971 bp.

The nucleotide sequence disclosed herein for vp19\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vp19\_1 demonstrated at least some similarity with sequences identified as AA716408 (zg64b02.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 398091 3', mRNA sequence) and T20711 (Human gene signature HUMGS01928). Based upon sequence similarity, vp19\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the vp19\_1 protein sequence centered around amino acid 23 of SEQ ID NO:76; due to its hydrophobic nature, this region (amino acids 20 to 32) could also be a leader/signal sequence, with the mature protein beginning at amino acid 33 of SEQ ID NO:76.

# 25 <u>Clone "vq1 1"</u>

10

15

20

30

A polynucleotide of the present invention has been identified as clone "vq1\_1". vq1\_1 was isolated from a human adult lung cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vq1\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vq1\_1 protein").

The nucleotide sequence of vq1\_1 as presently determined is reported in SEQ ID NO:77, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vq1\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:78. Amino acids 17 to 29

of SEQ ID NO:78 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 30. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vq1\_1 protein. If a "T" residue were inserted between nucleotides 332 and 333 of SEQ ID NO:77, nucleotides 54 to 496 of the resulting nucleotide sequence would encode a protein having an amino acid sequence reported as SEQ ID NO:132.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vq1\_1 should be approximately 873 bp.

The nucleotide sequence disclosed herein for vq1\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vq1\_1 demonstrated at least some similarity with sequences identified as No hits were found in the databases. The TopPredII computer program predicts an additional potential transmembrane domain within the vq1\_1 protein sequence, extending from about amino acid 36 to about amino acid 76 of SEQ ID NO:78. The nucleotide sequence of vq1\_1 indicates that it may contain an Alu repetitive element.

# Clone "vp14 1"

10

15

20

25

A polynucleotide of the present invention has been identified as clone "vp14\_1". vp14\_1 was isolated from a human adult prostate cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. vp14\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "vp14\_1 protein").

The nucleotide sequence of vp14\_1 as presently determined is reported in SEQ ID NO:79, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the vp14\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:80. Amino acids 5 to 17 of SEQ ID NO:80 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 18. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the vp14\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone vp14\_1 should be approximately 1355 bp.

The nucleotide sequence disclosed herein for vp14\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. vp14\_1 demonstrated at least some similarity with sequences identified as AI052724 (oz27a12.x1 Soares\_total\_fetus\_Nb2HF8\_9w Homo sapiens clone IMAGE:1676542 3' similar to SW:YQJQ\_BACSU P54554 HYPOTHETICAL OXIDOREDUCTASE IN GLNQ-ANSR INTERGENIC REGION; mRNA sequence) and T20001 (Human gene signature HUMGS01138). The predicted amino acid sequence disclosed herein for vp14\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted vp14\_1 protein demonstrated at least some similarity to sequences identified as R61477 (Clavulanic acid dehydrogenase sequence) and Z99116 (similar to ketoacyl reductase [Bacillus subtilis]). The predicted vp14\_1 protein shows some amino acid similarity to various dehydrogenases due to the presence of a short-chain alcohol dehydrogenase family signature at amino acids 51 to 240 of SEQ ID NO:80, as detected by motifs and hidden markov model analysis. Based upon sequence similarity, vp14\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts four additional potential transmembrane domains within the vp14\_1 protein sequence, centered around amino acids 55, 195, 230, and 300 of SEQ ID NO:80, respectively.

#### **Deposit of Clones**

10

15

20

25

30

Clones vb11\_1, vb12\_1, vb14\_1, ve11\_1, vf2\_1, vg2\_1, vj1\_1, and vl1\_1 were deposited on August 20, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98846, from which each clone comprising a particular polynucleotide is obtainable.

Clone vk2\_1 was deposited on August 20, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and was given the accession number 98838, from which the vk2\_1 clone comprising a particular polynucleotide is obtainable.

Clones vb21\_1, vc35\_1, vc36\_1, vc38\_1, vc39\_1, vc40\_1, vc46\_1, vc49\_1, vc50\_1, vc51\_1, and vc52\_1 were deposited on September 2, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98862, from which each clone comprising a particular polynucleotide is obtainable.

Clones vc33\_1, vc34\_1, vc47\_1, vc54\_1, vc57\_1, ve13\_1, ve16\_1, vf3\_1, vj2\_1, vp7\_1, and vp8\_1 were deposited on September 22, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98886, from which each clone comprising a particular polynucleotide is obtainable.

10

15

20

25

30

Clones vb22\_1, vc48\_1, and vp3\_1 were deposited on October 16, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98933, from which each clone comprising a particular polynucleotide is obtainable.

Clones vc61\_1, vp15\_1, vp17\_1, vp19\_1, and vq1\_1 were deposited on December 23, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 207012, from which each clone comprising a particular polynucleotide is obtainable.

Clone vp14\_1 was deposited on December 23, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and was given the accession number 207011, from which the vp14\_1 clone comprising a particular polynucleotide is obtainable.

All restrictions on the availability to the public of the deposited material will be irrevocably removed upon the granting of the patent, except for the requirements specified in 37 C.F.R. § 1.808(b), and the term of the deposit will comply with 37 C.F.R. § 1.806.

Each clone has been transfected into separate bacterial cells (*E. coli*) in this composite deposit. Each clone can be removed from the vector in which it was deposited by performing an EcoRI/NotI digestion (5' site, EcoRI; 3' site, NotI) to produce the appropriate fragment for such clone. Each clone was deposited in either the pED6 or pNOTs vector depicted in Figures 1A and 1B, respectively. The pED6dpc2 vector

("pED6") was derived from pED6dpc1 by insertion of a new polylinker to facilitate cDNA cloning (Kaufman et al., 1991, Nucleic Acids Res. 19: 4485-4490); the pNOTs vector was derived from pMT2 (Kaufman et al., 1989, Mol. Cell. Biol. 9: 946-958) by deletion of the DHFR sequences, insertion of a new polylinker, and insertion of the M13 origin of replication in the ClaI site. In some instances, the deposited clone can become "flipped" (i.e., in the reverse orientation) in the deposited isolate. In such instances, the cDNA insert can still be isolated by digestion with EcoRI and NotI. However, NotI will then produce the 5' site and EcoRI will produce the 3' site for placement of the cDNA in proper orientation for expression in a suitable vector. The cDNA may also be expressed from the vectors in which they were deposited.

Bacterial cells containing a particular clone can be obtained from the composite deposit as follows:

An oligonucleotide probe or probes should be designed to the sequence that is known for that particular clone. This sequence can be derived from the sequences provided herein, or from a combination of those sequences. The sequence of an oligonucleotide probe that was used to isolate or to sequence each full-length clone is identified below, and should be most reliable in isolating the clone of interest.

	Clone	Probe Sequence
20	vb11_1	SEQ ID NO:81
	vb12_1	SEQ ID NO:82
	vb14_1	SEQ ID NO:83
	vel1_1	SEQ ID NO:84
	vf2_1	SEQ ID NO:85
25	vg2_1	SEQ ID NO:86
	vj1_1	SEQ ID NO:87
	vl1_1	SEQ ID NO:88
	vk2_1	SEQ ID NO:89
	vb21_1	SEQ ID NO:90
30	vc35_1	SEQ ID NO:91
	vc36_1	SEQ ID NO:92
	vc38_1	SEQ ID NO:93
	vc39_1	SEQ ID NO:94
	vc40_1	SEQ ID NO:95

10

15

	vc46_1	SEQ ID NO:96
	vc49_1	SEQ ID NO:97
	vc50_1	SEQ ID NO:98
	vc51_1	SEQ ID NO:99
5	vc52_1	SEQ ID NO:100
	vc33_1	SEQ ID NO:101
	vc34_1	SEQ ID NO:102
	vc47_1	SEQ ID NO:103
	vc54_1	SEQ ID NO:104
10	vc57_1	SEQ ID NO:105
	ve13_1	SEQ ID NO:106
	ve16_1	SEQ ID NO:107
	vf3_1	SEQ ID NO:108
	vj2_1	SEQ ID NO:109
15	vp7_1	SEQ ID NO:110
	vp8_1	SEQ ID NO:111
	vb22_1	SEQ ID NO:112
	vc48_1	SEQ ID NO:113
	vp3_1	SEQ ID NO:114
20	vc61_1	SEQ ID NO:115
	vp15_1	SEQ ID NO:116
	vp17_1	SEQ ID NO:117
	vp19_1	SEQ ID NO:118
	vq1_1	SEQ ID NO:119
25	vp14_1	SEQ ID NO:120

30

In the sequences listed above which include an N at position 2, that position is occupied in preferred probes/primers by a biotinylated phosphoaramidite residue rather than a nucleotide (such as, for example, that produced by use of biotin phosphoramidite (1-dimethoxytrityloxy-2-(N-biotinyl-4-aminobutyl)-propyl-3-O-(2-cyanoethyl)-(N,N-diisopropyl)-phosphoramadite) (Glen Research, cat. no. 10-1953)).

The design of the oligonucleotide probe should preferably follow these parameters:

(a) It should be designed to an area of the sequence which has the fewest ambiguous bases ("N's"), if any;

- (b) It should be designed to have a T<sub>m</sub> of approx. 80 ° C (assuming 2° for each A or T and 4 degrees for each G or C).
- The oligonucleotide should preferably be labeled with γ-32P ATP (specific activity 6000 Ci/mmole) and T4 polynucleotide kinase using commonly employed techniques for labeling oligonucleotides. Other labeling techniques can also be used. Unincorporated label should preferably be removed by gel filtration chromatography or other established methods. The amount of radioactivity incorporated into the probe should be quantitated by measurement in a scintillation counter. Preferably, specific activity of the resulting probe should be approximately 4e+6 dpm/pmole.

The bacterial culture containing the pool of full-length clones should preferably be thawed and 100 µl of the stock used to inoculate a sterile culture flask containing 25 ml of sterile L-broth containing ampicillin at 100 µg/ml. The culture should preferably be grown to saturation at 37°C, and the saturated culture should preferably be diluted in fresh L-broth. Aliquots of these dilutions should preferably be plated to determine the dilution and volume which will yield approximately 5000 distinct and well-separated colonies on solid bacteriological media containing L-broth containing ampicillin at 100 µg/ml and agar at 1.5% in a 150 mm petri dish when grown overnight at 37°C. Other known methods of obtaining distinct, well-separated colonies can also be employed.

15

20

Standard colony hybridization procedures should then be used to transfer the colonies to nitrocellulose filters and lyse, denature and bake them.

The filter is then preferably incubated at 65°C for 1 hour with gentle agitation in 6X SSC (20X stock is 175.3 g NaCl/liter, 88.2 g Na citrate/liter, adjusted to pH 7.0 with NaOH) containing 0.5% SDS, 100 µg/ml of yeast RNA, and 10 mM EDTA (approximately 10 mL per 150 mm filter). Preferably, the probe is then added to the hybridization mix at a concentration greater than or equal to 1e+6 dpm/mL. The filter is then preferably incubated at 65°C with gentle agitation overnight. The filter is then preferably washed in 500 mL of 2X SSC/0.5% SDS at room temperature without agitation, preferably followed by 500 mL of 2X SSC/0.1% SDS at room temperature with gentle shaking for 15 minutes. A third wash with 0.1X SSC/0.5% SDS at 65°C for 30 minutes to 1 hour is optional. The filter is then preferably dried and subjected to autoradiography for sufficient time to visualize the positives on the X-ray film. Other known hybridization methods can also be employed.

The positive colonies are picked, grown in culture, and plasmid DNA isolated using standard procedures. The clones can then be verified by restriction analysis, hybridization analysis, or DNA sequencing.

Fragments of the proteins of the present invention which are capable of exhibiting biological activity are also encompassed by the present invention. Fragments of the protein may be in linear form or they may be cyclized using known methods, for example, as described in H.U. Saragovi, et al., Bio/Technology 10, 773-778 (1992) and in R.S. McDowell, et al., J. Amer. Chem. Soc. 114, 9245-9253 (1992), both of which are incorporated herein by reference. Such fragments may be fused to carrier molecules such as immunoglobulins for many purposes, including increasing the valency of protein binding sites. For example, fragments of the protein may be fused through "linker" sequences to the Fc portion of an immunoglobulin. For a bivalent form of the protein, such a fusion could be to the Fc portion of an IgG molecule. Other immunoglobulin isotypes may also be used to generate such fusions. For example, a protein - IgM fusion would generate a decavalent form of the protein of the invention.

10

15

20

25

The present invention also provides both full-length and mature forms of the disclosed proteins. The full-length form of the such proteins is identified in the sequence listing by translation of the nucleotide sequence of each disclosed clone. The mature form(s) of such protein may be obtained by expression of the disclosed full-length polynucleotide (preferably those deposited with the ATCC) in a suitable mammalian cell or other host cell. The sequence(s) of the mature form(s) of the protein may also be determinable from the amino acid sequence of the full-length form.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that

has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

The chromosomal location corresponding to the polynucleotide sequences disclosed herein may also be determined, for example by hybridizing appropriately labeled polynucleotides of the present invention to chromosomes in situ. It may also be possible to determine the corresponding chromosomal location for a disclosed polynucleotide by identifying significantly similar nucleotide sequences in public databases, such as expressed sequence tags (ESTs), that have already been mapped to particular chromosomal locations. For at least some of the polynucleotide sequences disclosed herein, public database sequences having at least some similarity to the polynucleotide of the present invention have been listed by database accession number. Searches using the GenBank accession numbers of these public database sequences can then be performed at an Internet site provided by the National Center for Biotechnology Information having the address http://www.ncbi.nlm.nih.gov/UniGene/, in order to identify "UniGene clusters" of overlapping sequences. Many of the "UniGene clusters" so identified will already have been mapped to particular chromosomal sites.

10

15

20

25

30

Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, Trends Pharmacol. Sci. 15(7): 250-254; Lavarosky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein). The desired change in gene expression can also be achieved through the use of double-stranded ribonucleotide molecules having some complementarity to the mRNA transcribed from the gene, and which interfere with the transcription, stability, or expression of the mRNA ("RNA intereference" or "RNAi"; Fire et al., 1998, Nature 391 (6669): 806-811; Montgomery et al., 1998, Proc. Natl. Acad. Sci. USA 95 (26): 15502-15507; and Sharp, 1999, Genes Dev. 13 (2): 139-141; all of which are incorporated by reference herein). Transgenic animals that have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are

also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished through insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the protein product(s) of the corresponding gene(s).

10

15

20

25

30

Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms, part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information. For example, the TopPredII computer program can be used to predict the location of transmembrane domains in an amino acid sequence, domains which are described by the location of the center of the transmembrane domain, with at least ten transmembrane amino acids on each side of the reported central residue(s).

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25%(more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are

proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

5

10

15

20

25

30

In particular, sequence identity may be determined using WU-BLAST (Washington University BLAST) version 2.0 software, which builds upon WU-BLAST version 1.4, which in turn is based on the public domain NCBI-BLAST version 1.4 (Altschul and Gish, 1996, Local alignment statistics, Doolittle ed., Methods in Enzymology 266: 460-480; Altschul et al., 1990, Basic local alignment search tool, Journal of Molecular Biology 215: 403-410; Gish and States, 1993, Identification of protein coding regions by database similarity search, Nature Genetics 3: 266-272; Karlin and Altschul, 1993, Applications and statistics for multiple high-scoring segments in molecular sequences, Proc. Natl. Acad. Sci. USA 90: 5873-5877; all of which are incorporated by reference herein). WU-BLAST version 2.0 executable programs for several UNIX platforms can be downloaded from ftp://blast.wustl.edu/blast/executables. The complete suite of search programs (BLASTP, BLASTN, BLASTX, TBLASTN, and TBLASTX) is provided at that site, in addition to several support programs. WU-BLAST 2.0 is copyrighted and may not be sold or redistributed in any form or manner without the express written consent of the author; but the posted executables may otherwise be freely used for commercial, nonprofit, or academic purposes. In all search programs in the suite -- BLASTP, BLASTN, BLASTX, TBLASTN and TBLASTX -- the gapped alignment routines are integral to the database search itself, and thus yield much better sensitivity and selectivity while producing the more easily interpreted output. Gapping can optionally be turned off in all of these programs, if desired. The default penalty (Q) for a gap of length one is Q=9 for proteins and BLASTP, and Q=10 for BLASTN, but may be changed to any integer value including zero, one through eight, nine, ten, eleven, twelve through twenty, twenty-one through fifty, fifty-one through one hundred, etc. The default per-residue penalty for extending a gap (R) is R=2 for proteins and BLASTP, and R=10 for BLASTN, but may be changed to any integer value including zero, one, two, three, four, five, six, seven, eight, nine, ten, eleven, twelve through twenty, twenty-one through fifty, fifty-one through one hundred, etc. Any combination of values for Q and R can be used in order to align sequences so as to maximize overlap and identity while minimizing sequence gaps.

The default amino acid comparison matrix is BLOSUM62, but other amino acid comparison matrices such as PAM can be utilized.

Species homologues of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide. Preferably, polynucleotide species homologues have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% identity) with the given polynucleotide, and protein species homologues have at least 30% sequence identity (more preferably, at least 45% identity; most preferably at least 60% identity) with the given protein, where sequence identity is determined by comparing the nucleotide sequences of the polynucleotides or the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Species homologues may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species. Preferably, species homologues are those isolated from mammalian species. Most preferably, species homologues are those isolated from certain mammalian species such as, for example, Pan troglodytes, Gorilla gorilla, Pongo pygmaeus, Hylobates concolor, Macaca mulatta, Papio papio, Papio hamadryas, Cercopithecus aethiops, Cebus capucinus, Aotus trivirgatus, Sanguinus oedipus, Microcebus murinus, Mus musculus, Rattus norvegicus, Cricetulus griseus, Felis catus, Mustela vison, Canis familiaris, Oryctolagus cuniculus, Bos taurus, Ovis aries, Sus scrofa, and Equus caballus, for which genetic maps have been created allowing the identification of syntenic relationships between the genomic organization of genes in one species and the genomic organization of the related genes in another species (O'Brien and Seuánez, 1988, Ann. Rev. Genet. 22: 323-351; O'Brien et al., 1993, Nature Genetics 3:103-112; Johansson et al., 1995, Genomics 25: 682-690; Lyons et al., 1997, Nature Genetics 15: 47-56; O'Brien et al., 1997, Trends in Genetics 13(10): 393-399; Carver and Stubbs, 1997, Genome Research 7:1123-1137; all of which are incorporated by reference herein).

10

15

20

25

30

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotides which also encode proteins which are identical or have significantly similar sequences to those encoded by the disclosed polynucleotides. Preferably, allelic variants have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90%

identity) with the given polynucleotide, where sequence identity is determined by comparing the nucleotide sequences of the polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps. Allelic variants may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from individuals of the appropriate species.

The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

5

10

The present invention also includes polynucleotides that hybridize under reduced stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example, conditions M-R.

		T	т		
	Stringency Condition	Polynucleotide Hybrid	Hybrid Length (bp)‡	Hybridization Temperature and Buffer <sup>†</sup>	Wash Temperature and Buffer <sup>1</sup>
5	Α	DNA:DNA	≥ 50	65°C; 1xSSC -or- 42°C; 1xSSC, 50% formamide	65°C; 0.3xSSC
	В	DNA:DNA	<50	T <sub>8</sub> *; 1xSSC	T <sub>B</sub> *; 1xSSC
	С	DNA:RNA	≥ 50	67°C; 1xSSC -or- 45°C; 1xSSC, 50% formamide	67°C; 0.3xSSC
	D	DNA:RNA	<50	T <sub>D</sub> *; 1xSSC	T <sub>D</sub> *; 1xSSC
	E	RNA:RNA	≥ 50	70°C; 1xSSC -or- 50°C; 1xSSC, 50% formamide	70°C; 0.3xSSC
	F	RNA:RNA	<50	T <sub>F</sub> *; 1xSSC	T <sub>F</sub> *; 1xSSC
	G	DNA:DNA	≥ 50	65°C; 4xSSC -or- 42°C; 4xSSC, 50% formamide	65°C; 1xSSC
10	Н	DNA:DNA	<50	T <sub>H</sub> *; 4xSSC	T <sub>H</sub> *; 4xSSC
	I	DNA:RNA	≥ 50	67°C; 4xSSC -or- 45°C; 4xSSC, 50% formamide	67°C; 1xSSC
	J	DNA:RNA	<50	T <sub>j</sub> *; 4xSSC	Tj*; 4xSSC
	K	RNA:RNA	≥ 50	70°C; 4xSSC -or- 50°C; 4xSSC, 50% formamide	67°C; 1xSSC
	L	RNA:RNA	<50	T <sub>L</sub> *; 2xSSC	T <sub>L</sub> *; 2xSSC
15	М	DNA:DNA	≥ 50	50°C; 4xSSC -or- 40°C; 6xSSC, 50% formamide	50°C; 2xSSC
	N	DNA:DNA	<50	T <sub>N</sub> *; 6xSSC	T <sub>N</sub> *; 6xSSC
:	0	DNA:RNA	≥ 50	55°C; 4xSSC -or- 42°C; 6xSSC, 50% formamide	55°C; 2xSSC
	P	DNA:RNA	<50	T <sub>p</sub> *; 6xSSC	T <sub>P</sub> *; 6xSSC
	Q	RNA:RNA	≥ 50	60°C; 4xSSC -or- 45°C; 6xSSC, 50% formamide	60°C; 2xSSC
20	R	RNA:RNA	<50	T <sub>R</sub> *; 4xSSC	T <sub>R</sub> *; 4xSSC

<sup>\*:</sup> The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.

25

t: SSPE (1xSSPE is 0.15M NaCl, 10mM NaH<sub>2</sub>PO<sub>4</sub>, and 1.25mM EDTA, pH 7.4) can be substituted for SSC (1xSSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.

T<sub>B</sub> - T<sub>R</sub>: The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10°C less than the melting temperature (T<sub>m</sub>) of the hybrid, where T<sub>m</sub> is determined according to the following equations. For hybrids less than 18 base pairs in length, T<sub>m</sub>(°C) = 2(# of A + T bases) + 4(# of G + C bases). For hybrids between 18 and 49 base pairs in length, T<sub>m</sub>(°C) = 81.5 + 16.6(log<sub>10</sub>[Na\*]) + 0.41(%G+C) - (600/N), where N is the number of bases in the hybrid, and [Na\*] is the concentration of sodium ions in the hybridization buffer ([Na\*] for 1xSSC = 0.165 M).

Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and *Current Protocols in Molecular Biology*, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25%(more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

10

15

20

25

30

The isolated polynucleotide endcoing the protein of the invention may be operably linked to an expression control sequence such as the pMT2 or pED expression vectors disclosed in Kaufman *et al.*, Nucleic Acids Res. 19, 4485-4490 (1991), in order to produce the protein recombinantly. Many suitable expression control sequences are known in the art. General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, Methods in Enzymology 185, 537-566 (1990). As defined herein "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the protein is expressed by a host cell which has been transformed (transfected) with the ligated polynucleotide/expression control sequence.

A number of types of cells may act as suitable host cells for expression of the protein. Mammalian host cells include, for example, monkey COS cells, Chinese Hamster Ovary (CHO) cells, human kidney 293 cells, human epidermal A431 cells, human Colo205 cells, 3T3 cells, CV-1 cells, other transformed primate cell lines, normal diploid cells, cell strains derived from in vitro culture of primary tissue, primary explants, HeLa cells, mouse L cells, BHK, HL-60, U937, HaK or Jurkat cells.

Alternatively, it may be possible to produce the protein in lower eukaryotes such as yeast or in prokaryotes such as bacteria. Potentially suitable yeast strains include Saccharomyces cerevisiae, Schizosaccharomyces pombe, Kluyveromyces strains, Candida, or any yeast strain capable of expressing heterologous proteins. Potentially suitable bacterial strains include Escherichia coli, Bacillus subtilis, Salmonella typhimurium, or any bacterial

strain capable of expressing heterologous proteins. If the protein is made in yeast or bacteria, it may be necessary to modify the protein produced therein, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain the functional protein. Such covalent attachments may be accomplished using known chemical or enzymatic methods.

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, e.g., Invitrogen, San Diego, California, U.S.A. (the MaxBac® kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "transformed."

10

15

20

25

30

The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (i.e., from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, heparin-toyopearl® or Cibacrom blue 3GA Sepharose®; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography.

Alternatively, the protein of the invention may also be expressed in a form which will facilitate purification. For example, it may be expressed as a fusion protein, such as those of maltose binding protein (MBP), glutathione-S-transferase (GST) or thioredoxin (TRX). Kits for expression and purification of such fusion proteins are commercially available from New England BioLabs (Beverly, MA), Pharmacia (Piscataway, NJ) and Invitrogen Corporation (Carlsbad, CA), respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope ("Flag") is commercially available from the Eastman Kodak Company (New Haven, CT).

Finally, one or more reverse-phase high performance liquid chromatography (RP-HPLC) steps employing hydrophobic RP-HPLC media, e.g., silica gel having pendant methyl or other aliphatic groups, can be employed to further purify the protein. Some or all of the foregoing purification steps, in various combinations, can also be employed to provide a substantially homogeneous isolated recombinant protein. The protein thus purified is substantially free of other mammalian proteins and is defined in accordance with the present invention as an "isolated protein."

The protein of the invention may also be expressed as a product of transgenic animals, e.g., as a component of the milk of transgenic cows, goats, pigs, or sheep which are characterized by somatic or germ cells containing a nucleotide sequence encoding the protein.

10

15

20

25

30

The protein may also be produced by known conventional chemical synthesis. Methods for constructing the proteins of the present invention by synthetic means are known to those skilled in the art. The synthetically-constructed protein sequences, by virtue of sharing primary, secondary or tertiary structural and/or conformational characteristics with proteins may possess biological properties in common therewith, including protein activity. Thus, they may be employed as biologically active or immunological substitutes for natural, purified proteins in screening of therapeutic compounds and in immunological processes for the development of antibodies.

The proteins provided herein also include proteins characterized by amino acid sequences similar to those of purified proteins but into which modification are naturally provided or deliberately engineered. For example, modifications in the peptide or DNA sequences can be made by those skilled in the art using known techniques. Modifications of interest in the protein sequences may include the alteration, substitution, replacement, insertion or deletion of a selected amino acid residue in the coding sequence. For example, one or more of the cysteine residues may be deleted or replaced with another amino acid to alter the conformation of the molecule. Techniques for such alteration, substitution, replacement, insertion or deletion are well known to those skilled in the art (see, e.g., U.S. Patent No. 4,518,584). Preferably, such alteration, substitution, replacement, insertion or deletion retains the desired activity of the protein.

Other fragments and derivatives of the sequences of proteins which would be expected to retain protein activity in whole or in part and may thus be useful for screening or other immunological methodologies may also be easily made by those skilled in the art

given the disclosures herein. Such modifications are believed to be encompassed by the present invention.

# **USES AND BIOLOGICAL ACTIVITY**

5

10

15

20

25

30

The polynucleotides and proteins of the present invention are expected to exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

## Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, those described in Gyuris et al., 1993, Cell 75: 791-803 and in Rossi et al., 1997, Proc. Natl. Acad. Sci. USA 94: 8405-8410, all of which are incorporated by reference herein) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

#### Nutritional Uses

10

20

25

30

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

# Cytokine and Cell Proliferation/Differentiation Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may

induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor-dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

10

15

20

25

30

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon γ, Schreiber, R.D. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6 - Nordan, R. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991;

Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immunol. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

# 15 Immune Stimulating or Suppressing Activity

10

20

25

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease.

Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

5

10

15

20

25

30

Using the proteins of the invention it may also be possible to regulate immune responses in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term

tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

5

10

15

20

25

30

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins *in vivo* as described in Lenschow *et al.*, Science 257:789-792 (1992) and Turka *et al.*, Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function *in vivo* on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune

response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells *in vitro* with viral antigenpulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the *in vitro* activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells *in vivo*.

15

20

25

30

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I  $\alpha$  chain protein and  $\beta_2$ 

microglobulin protein or an MHC class II  $\alpha$  chain protein and an MHC class II  $\beta$  chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

1.0

30

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowmanet al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: *In vitro* antibody production, Mond, J.J. and Brunswick, M. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek,

D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

25

30

5

10

15

20

#### Hematopoiesis Regulating Activity

A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid

cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either *in-vivo* or *ex-vivo* (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

10

15

20

25

30

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and

Allen, T. In *Culture of Hematopoietic Cells*. R.I. Freshney, *et al.* eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In *Culture of Hematopoietic Cells*. R.I. Freshney, *et al.* eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

5

10

15

20

25

30

### **Tissue Growth Activity**

A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. *De novo* bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and

in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

10

15

20

25

30

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, *i.e.* for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation

of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon); International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

# 20 <u>Activin/Inhibin Activity</u>

5

10

15

25

A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin  $\alpha$  family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- $\beta$  group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

### Chemotactic/Chemokinetic Activity

10

15

20

25

30

A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al.

APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

### Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

### 20 <u>Receptor/Ligand Activity</u>

5

10

25

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in:Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

# 10 <u>Anti-Inflammatory Activity</u>

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

25

15

20

#### Cadherin/Tumor Invasion Suppressor Activity

Cadherins are calcium-dependent adhesion molecules that appear to play major roles during development, particularly in defining specific cell types. Loss or alteration of normal cadherin expression can lead to changes in cell adhesion properties linked to tumor growth and metastasis. Cadherin malfunction is also implicated in other human diseases, such as pemphigus vulgaris and pemphigus foliaceus (auto-immune blistering skin diseases), Crohn's disease, and some developmental abnormalities.

The cadherin superfamily includes well over forty members, each with a distinct pattern of expression. All members of the superfamily have in common conserved

extracellular repeats (cadherin domains), but structural differences are found in other parts of the molecule. The cadherin domains bind calcium to form their tertiary structure and thus calcium is required to mediate their adhesion. Only a few amino acids in the first cadherin domain provide the basis for homophilic adhesion; modification of this recognition site can change the specificity of a cadherin so that instead of recognizing only itself, the mutant molecule can now also bind to a different cadherin. In addition, some cadherins engage in heterophilic adhesion with other cadherins.

E-cadherin, one member of the cadherin superfamily, is expressed in epithelial cell types. Pathologically, if E-cadherin expression is lost in a tumor, the malignant cells become invasive and the cancer metastasizes. Transfection of cancer cell lines with polynucleotides expressing E-cadherin has reversed cancer-associated changes by returning altered cell shapes to normal, restoring cells' adhesiveness to each other and to their substrate, decreasing the cell growth rate, and drastically reducing anchorage-independent cell growth. Thus, reintroducing E-cadherin expression reverts carcinomas to a less advanced stage. It is likely that other cadherins have the same invasion suppressor role in carcinomas derived from other tissue types. Therefore, proteins of the present invention with cadherin activity, and polynucleotides of the present invention encoding such proteins, can be used to treat cancer. Introducing such proteins or polynucleotides into cancer cells can reduce or eliminate the cancerous changes observed in these cells by providing normal cadherin expression.

10

15

20

25

30

Cancer cells have also been shown to express cadherins of a different tissue type than their origin, thus allowing these cells to invade and metastasize in a different tissue in the body. Proteins of the present invention with cadherin activity, and polynucleotides of the present invention encoding such proteins, can be substituted in these cells for the inappropriately expressed cadherins, restoring normal cell adhesive properties and reducing or eliminating the tendency of the cells to metastasize.

Additionally, proteins of the present invention with cadherin activity, and polynucleotides of the present invention encoding such proteins, can used to generate antibodies recognizing and binding to cadherins. Such antibodies can be used to block the adhesion of inappropriately expressed tumor-cell cadherins, preventing the cells from forming a tumor elsewhere. Such an anti-cadherin antibody can also be used as a marker for the grade, pathological type, and prognosis of a cancer, i.e. the more progressed the cancer, the less cadherin expression there will be, and this decrease in cadherin expression can be detected by the use of a cadherin-binding antibody.

Fragments of proteins of the present invention with cadherin activity, preferably a polypeptide comprising a decapeptide of the cadherin recognition site, and polynucleotides of the present invention encoding such protein fragments, can also be used to block cadherin function by binding to cadherins and preventing them from binding in ways that produce undesirable effects. Additionally, fragments of proteins of the present invention with cadherin activity, preferably truncated soluble cadherin fragments which have been found to be stable in the circulation of cancer patients, and polynucleotides encoding such protein fragments, can be used to disturb proper cell-cell adhesion.

Assays for cadherin adhesive and invasive suppressor activity include, without limitation, those described in: Hortsch et al. J Biol Chem 270 (32): 18809-18817, 1995; Miyaki et al. Oncogene 11: 2547-2552, 1995; Ozawa et al. Cell 63: 1033-1038, 1990.

#### **Tumor Inhibition Activity**

5

10

15

20

25

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via antibody-dependent cell-mediated cytotoxicity (ADCC)). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth.

#### Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or caricadic cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s);

effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

#### **ADMINISTRATION AND DOSING**

10

20

25

30

A protein of the present invention (from whatever source derived, including without limitation from recombinant and non-recombinant sources) may be used in a pharmaceutical composition when combined with a pharmaceutically acceptable carrier. Such a composition may also contain (in addition to protein and a carrier) diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredient(s). The characteristics of the carrier will depend on the route of administration. The pharmaceutical composition of the invention may also contain cytokines, lymphokines, or other hematopoietic factors such as M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IFN, TNF0, TNF1, TNF2, G-CSF, Meg-CSF, thrombopoietin, stem cell factor, and erythropoietin. The pharmaceutical composition may further contain other agents which either enhance the activity of the protein or compliment its activity or use in treatment. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with protein of the invention, or to minimize side effects. Conversely, protein of the present invention may be included in formulations of the particular cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent to minimize side effects of the cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent.

A protein of the present invention may be active in multimers (e.g., heterodimers or homodimers) or complexes with itself or other proteins. As a result, pharmaceutical

compositions of the invention may comprise a protein of the invention in such multimeric or complexed form.

The pharmaceutical composition of the invention may be in the form of a complex of the protein(s) of present invention along with protein or peptide antigens. The protein and/or peptide antigen will deliver a stimulatory signal to both B and T lymphocytes. B lymphocytes will respond to antigen through their surface immunoglobulin receptor. T lymphocytes will respond to antigen through the T cell receptor (TCR) following presentation of the antigen by MHC proteins. MHC and structurally related proteins including those encoded by class I and class II MHC genes on host cells will serve to present the peptide antigen(s) to T lymphocytes. The antigen components could also be supplied as purified MHC-peptide complexes alone or with co-stimulatory molecules that can directly signal T cells. Alternatively antibodies able to bind surface immunolgobulin and other molecules on B cells as well as antibodies able to bind the TCR and other molecules on T cells can be combined with the pharmaceutical composition of the invention.

10

15

20

25

30

The pharmaceutical composition of the invention may be in the form of a liposome in which protein of the present invention is combined, in addition to other pharmaceutically acceptable carriers, with amphipathic agents such as lipids which exist in aggregated form as micelles, insoluble monolayers, liquid crystals, or lamellar layers in aqueous solution. Suitable lipids for liposomal formulation include, without limitation, monoglycerides, diglycerides, sulfatides, lysolecithin, phospholipids, saponin, bile acids, and the like. Preparation of such liposomal formulations is within the level of skill in the art, as disclosed, for example, in U.S. Patent No. 4,235,871; U.S. Patent No. 4,501,728; U.S. Patent No. 4,837,028; and U.S. Patent No. 4,737,323, all of which are incorporated herein by reference.

As used herein, the term "therapeutically effective amount" means the total amount of each active component of the pharmaceutical composition or method that is sufficient to show a meaningful patient benefit, i.e., treatment, healing, prevention or amelioration of the relevant medical condition, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. When applied to an individual active ingredient, administered alone, the term refers to that ingredient alone. When applied to a combination, the term refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of protein of the present invention is administered to a mammal having a condition to be treated. Protein of the present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing cytokines, lymphokines or other hematopoietic factors. When co-administered with one or more cytokines, lymphokines or other hematopoietic factors, protein of the present invention may be administered either simultaneously with the cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering protein of the present invention in combination with cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors.

10

15

20

25

30

Administration of protein of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a variety of conventional ways, such as oral ingestion, inhalation, topical application or cutaneous, subcutaneous, intraperitoneal, parenteral or intravenous injection. Intravenous administration to the patient is preferred.

When a therapeutically effective amount of protein of the present invention is administered orally, protein of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical composition of the invention may additionally contain a solid carrier such as a gelatin or an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% protein of the present invention, and preferably from about 25 to 90% protein of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol, propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of protein of the present invention, and preferably from about 1 to 50% protein of the present invention.

When a therapeutically effective amount of protein of the present invention is administered by intravenous, cutaneous or subcutaneous injection, protein of the present

invention will be in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein solutions, having due regard to pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to protein of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art.

10

20

25

30

The amount of protein of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments which the patient has undergone. Ultimately, the attending physician will decide the amount of protein of the present invention with which to treat each individual patient. Initially, the attending physician will administer low doses of protein of the present invention and observe the patient's response. Larger doses of protein of the present invention may be administered until the optimal therapeutic effect is obtained for the patient, and at that point the dosage is not increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.01 µg to about 100 mg (preferably about 0.1ng to about 10 mg, more preferably about 0.1 µg to about 1 mg) of protein of the present invention per kg body weight.

The duration of intravenous therapy using the pharmaceutical composition of the present invention will vary, depending on the severity of the disease being treated and the condition and potential idiosyncratic response of each individual patient. It is contemplated that the duration of each application of the protein of the present invention will be in the range of 12 to 24 hours of continuous intravenous administration. Ultimately the attending physician will decide on the appropriate duration of intravenous therapy using the pharmaceutical composition of the present invention.

Protein of the invention may also be used to immunize animals to obtain polyclonal and monoclonal antibodies which specifically react with the protein. As used herein, the term "antibody" includes without limitation a polyclonal antibody, a monoclonal antibody, a chimeric antibody, a single-chain antibody, a CDR-grafted antibody, a humanized antibody, or fragments thereof which bind to the indicated protein.

Such term also includes any other species derived from an antibody or antibody sequence which is capable of binding the indicated protein.

Antibodies to a particular protein can be produced by methods well known to those skilled in the art. For example, monoclonal antibodies can be produced by generation of antibody-producing hybridomas in accordance with known methods (see for example, Goding, 1983, Monoclonal antibodies: principles and practice, Academic Press Inc., New York; and Yokoyama, 1992, "Production of Monoclonal Antibodies" in Current Protocols in Immunology, Unit 2.5, Greene Publishing Assoc. and John Wiley & Sons). Polyclonal sera and antibodies can be produced by inoculation of a mammalian subject with the relevant protein or fragments thereof in accordance with known methods. Fragments of antibodies, receptors, or other reactive peptides can be produced from the corresponding antibodies by cleavage of and collection of the desired fragments in accordance with known methods (see for example, Goding, supra; and Andrew et al., 1992, "Fragmentation of Immunoglobulins" in Current Protocols in Immunology, Unit 2.8, Greene Publishing Assoc. and John Wiley & Sons). Chimeric antibodies and single chain antibodies can also be produced in accordance with known recombinant methods (see for example, 5,169,939, 5,194,594, and 5,576,184). Humanized antibodies can also be made from corresponding murine antibodies in accordance with well known methods (see for example, U.S. Patent Nos. 5,530,101, 5,585,089, and 5,693,762). Additionally, human antibodies may be produced in non-human animals such as mice that have been genetically altered to express human antibody molecules (see for example Fishwild et al., 1996, Nature Biotechnology 14: 845-851; Mendez et al., 1997, Nature Genetics 15: 146-156 (erratum Nature Genetics 16: 410); and U.S. Patents 5,877,397 and 5,625,126). Such antibodies may be obtained using either the entire protein or fragments thereof as an immunogen. The peptide immunogens additionally may contain a cysteine residue at the carboxyl terminus, and are conjugated to a hapten such as keyhole limpet hemocyanin (KLH). Methods for synthesizing such peptides are known in the art, for example, as in R.P. Merrifield, J. Amer.Chem.Soc. 85, 2149-2154 (1963); J.L. Krstenansky, et al., FEBS Lett. 211, 10 (1987).

10

15

20

25

30

Monoclonal antibodies binding to the protein of the invention may be useful diagnostic agents for the immunodetection of the protein. Neutralizing monoclonal antibodies binding to the protein may also be useful therapeutics for both conditions associated with the protein and also in the treatment of some forms of cancer where

abnormal expression of the protein is involved. In the case of cancerous cells or leukemic cells, neutralizing monoclonal antibodies against the protein may be useful in detecting and preventing the metastatic spread of the cancerous cells, which may be mediated by the protein.

5

10

15

20

25

For compositions of the present invention which are useful for bone, cartilage, tendon or ligament regeneration, the therapeutic method includes administering the composition topically, systematically, or locally as an implant or device. When administered, the therapeutic composition for use in this invention is, of course, in a pyrogen-free, physiologically acceptable form. Further, the composition may desirably be encapsulated or injected in a viscous form for delivery to the site of bone, cartilage or tissue damage. Topical administration may be suitable for wound healing and tissue repair. Therapeutically useful agents other than a protein of the invention which may also optionally be included in the composition as described above, may alternatively or additionally, be administered simultaneously or sequentially with the composition in the methods of the invention. Preferably for bone and/or cartilage formation, the composition would include a matrix capable of delivering the protein-containing composition to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage and optimally capable of being resorbed into the body. Such matrices may be formed of materials presently in use for other implanted medical applications.

The choice of matrix material is based on biocompatibility, biodegradability, mechanical properties, cosmetic appearance and interface properties. The particular application of the compositions will define the appropriate formulation. Potential matrices for the compositions may be biodegradable and chemically defined calcium sulfate, tricalciumphosphate, hydroxyapatite, polylactic acid, polyglycolic acid and polyanhydrides. Other potential materials are biodegradable and biologically well-defined, such as bone or dermal collagen. Further matrices are comprised of pure proteins or extracellular matrix components. Other potential matrices are nonbiodegradable and chemically defined, such as sintered hydroxapatite, bioglass, aluminates, or other ceramics. Matrices may be comprised of combinations of any of the above mentioned types of material, such as polylactic acid and hydroxyapatite or collagen and tricalciumphosphate. The bioceramics may be altered in composition, such as in calciumaluminate-phosphate and processing to alter pore size, particle size, particle shape, and biodegradability.

Presently preferred is a 50:50 (mole weight) copolymer of lactic acid and glycolic acid in the form of porous particles having diameters ranging from 150 to 800 microns. In some applications, it will be useful to utilize a sequestering agent, such as carboxymethyl cellulose or autologous blood clot, to prevent the protein compositions from disassociating from the matrix.

A preferred family of sequestering agents is cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), including methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, and carboxymethylcellulose, the most preferred being cationic salts of carboxymethylcellulose (CMC). Other preferred sequestering agents include hyaluronic acid, sodium alginate, poly(ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer and poly(vinyl alcohol). The amount of sequestering agent useful herein is 0.5-20 wt%, preferably 1-10 wt% based on total formulation weight, which represents the amount necessary to prevent desorbtion of the protein from the polymer matrix and to provide appropriate handling of the composition, yet not so much that the progenitor cells are prevented from infiltrating the matrix, thereby providing the protein the opportunity to assist the osteogenic activity of the progenitor cells.

10

15

20

25

30

In further compositions, proteins of the invention may be combined with other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF- $\alpha$  and TGF- $\beta$ ), and insulin-like growth factor (IGF).

The therapeutic compositions are also presently valuable for veterinary applications. Particularly domestic animals and thoroughbred horses, in addition to humans, are desired patients for such treatment with proteins of the present invention.

The dosage regimen of a protein-containing pharmaceutical composition to be used in tissue regeneration will be determined by the attending physician considering various factors which modify the action of the proteins, e.g., amount of tissue weight desired to be formed, the site of damage, the condition of the damaged tissue, the size of a wound, type of damaged tissue (e.g., bone), the patient's age, sex, and diet, the severity of any infection, time of administration and other clinical factors. The dosage may vary with the type of matrix used in the reconstitution and with inclusion of other proteins in the pharmaceutical composition. For example, the addition of other known growth factors, such as IGF I (insulin like growth factor I), to the final composition, may also effect

the dosage. Progress can be monitored by periodic assessment of tissue/bone growth and/or repair, for example, X-rays, histomorphometric determinations and tetracycline labeling.

Polynucleotides of the present invention can also be used for gene therapy. Such polynucleotides can be introduced either *in vivo* or *ex vivo* into cells for expression in a mammalian subject. Polynucleotides of the invention may also be administered by other known methods for introduction of nucleic acid into a cell or organism (including, without limitation, in the form of viral vectors or naked DNA).

Cells may also be cultured *ex vivo* in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells.

Treated cells can then be introduced *in vivo* for therapeutic purposes.

Patent and literature references cited herein are incorporated by reference as if fully set forth.

#### What is claimed is:

1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:1;
- (b) the nucleotide sequence of SEQ ID NO:1 from nucleotide 683 to nucleotide 934;
- (c) the nucleotide sequence of the full-length protein coding sequence of clone vb11\_1 deposited with the ATCC under accession number 98846;
- (d) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vb11\_1 deposited with the ATCC under accession number 98846;
- (e) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:2;
- (f) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2, the fragment comprising eight contiguous amino acids of SEQ ID NO:2;
- (g) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d); and
- (h) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d), and that has a length that is at least 25% of the length of SEQ ID NO:1.
- 2. The polynucleotide of claim 1 wherein said polynucleotide is operably linked to at least one expression control sequence.
  - 3. A host cell transformed with the polynucleotide of claim 2.
  - 4. The host cell of claim 3, wherein said cell is a mammalian cell.
- 5. A process for producing a protein encoded by the polynucleotide of claim 2, which process comprises:

(a) growing a culture of a host cell in a suitable culture medium, wherein the host cell has been transformed with the polynucleotide of claim 2; and

- (b) purifying said protein from the culture.
- 6. A protein produced according to the process of claim 5.
- 7. An isolated polynucleotide encoding the protein of claim 6.
- 8. The polynucleotide of claim 7, wherein the polynucleotide comprises the cDNA insert of clone vb11\_1 deposited with the ATCC under accession number 98846.
- 9. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:2;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:2, the fragment comprising eight contiguous amino acids of SEQ ID NO:2; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vb11\_1 deposited with the ATCC under accession number 98846; the protein being substantially free from other mammalian proteins.
- 10. The protein of claim 9, wherein said protein comprises the amino acid sequence of SEQ ID NO:2.
- 11. A composition comprising the protein of claim 9 and a pharmaceutically acceptable carrier.
- 12. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:3;
  - (b) the nucleotide sequence of SEQ ID NO:3 from nucleotide 63 to nucleotide 482;
  - (c) the nucleotide sequence of SEQ ID NO:3 from nucleotide 201 to nucleotide 482:

(d) the nucleotide sequence of the full-length protein coding sequence of clone vb12\_1 deposited with the ATCC under accession number 98846;

- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vb12\_1 deposited with the ATCC under accession number 98846;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vb12\_1 deposited with the ATCC under accession number 98846;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vb12\_1 deposited with the ATCC under accession number 98846;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:4;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4, the fragment comprising eight contiguous amino acids of SEQ ID NO:4;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:3.
- 13. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:4;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:4, the fragment comprising eight contiguous amino acids of SEQ ID NO:4; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vb12\_1 deposited with the ATCC under accession number 98846; the protein being substantially free from other mammalian proteins.
- 14. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:5;
- (b) the nucleotide sequence of SEQ ID NO:5 from nucleotide 1195 to nucleotide 1527;
- (c) the nucleotide sequence of SEQ ID NO:5 from nucleotide 1468 to nucleotide 1527;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vb14\_1 deposited with the ATCC under accession number 98846;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vb14\_1 deposited with the ATCC under accession number 98846;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vb14\_1 deposited with the ATCC under accession number 98846;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vb14\_1 deposited with the ATCC under accession number 98846;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:6;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6, the fragment comprising eight contiguous amino acids of SEQ ID NO:6;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:5.
- 15. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:6;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:6, the fragment comprising eight contiguous amino acids of SEQ ID NO:6; and

(c) the amino acid sequence encoded by the cDNA insert of clone vb14\_1 deposited with the ATCC under accession number 98846; the protein being substantially free from other mammalian proteins.

- 16. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:7;
  - (b) the nucleotide sequence of SEQ ID NO:7 from nucleotide 82 to nucleotide 294;
  - (c) the nucleotide sequence of SEQ ID NO:7 from nucleotide 109 to nucleotide 294;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vell\_1 deposited with the ATCC under accession number 98846;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone ve11\_1 deposited with the ATCC under accession number 98846;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone ve11\_1 deposited with the ATCC under accession number 98846;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone ve11\_1 deposited with the ATCC under accession number 98846;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:8;
  - (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8, the fragment comprising eight contiguous amino acids of SEQ ID NO:8;
  - (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
  - (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:7.

17. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:8;
- (b) a fragment of the amino acid sequence of SEQ ID NO:8, the fragment comprising eight contiguous amino acids of SEQ ID NO:8; and
- (c) the amino acid sequence encoded by the cDNA insert of clone ve11\_1 deposited with the ATCC under accession number 98846; the protein being substantially free from other mammalian proteins.
- 18. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:9;
  - (b) the nucleotide sequence of SEQ ID NO:9 from nucleotide 22 to nucleotide 468;
  - (c) the nucleotide sequence of SEQ ID NO:9 from nucleotide 118 to nucleotide 468;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vf2\_1 deposited with the ATCC under accession number 98846;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vf2\_1 deposited with the ATCC under accession number 98846;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vf2\_1 deposited with the ATCC under accession number 98846;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vf2\_1 deposited with the ATCC under accession number 98846;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:10;
  - (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10, the fragment comprising eight contiguous amino acids of SEQ ID NO:10;
  - (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and

(k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEO ID NO:9.

- 19. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:10;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:10, the fragment comprising eight contiguous amino acids of SEQ ID NO:10; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vf2\_1 deposited with the ATCC under accession number 98846; the protein being substantially free from other mammalian proteins.
- 20. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:11;
  - (b) the nucleotide sequence of SEQ ID NO:11 from nucleotide 124 to nucleotide 1641;
  - (c) the nucleotide sequence of SEQ ID NO:11 from nucleotide 262 to nucleotide 1641;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vg2\_1 deposited with the ATCC under accession number 98846;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vg2\_1 deposited with the ATCC under accession number 98846;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vg2\_1 deposited with the ATCC under accession number 98846;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vg2\_1 deposited with the ATCC under accession number 98846;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:12;

(i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12, the fragment comprising eight contiguous amino acids of SEQ ID NO:12;

- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:11.
- 21. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:12;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:12, the fragment comprising eight contiguous amino acids of SEQ ID NO:12; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vg2\_1 deposited with the ATCC under accession number 98846; the protein being substantially free from other mammalian proteins.
- 22. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:13;
  - (b) the nucleotide sequence of SEQ ID NO:13 from nucleotide 380 to nucleotide 892;
  - (c) the nucleotide sequence of SEQ ID NO:13 from nucleotide 416 to nucleotide 892;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vj1\_1 deposited with the ATCC under accession number 98846;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vj1\_1 deposited with the ATCC under accession number 98846:
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vj1\_1 deposited with the ATCC under accession number 98846;

(g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vj1\_1 deposited with the ATCC under accession number 98846;

- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:14;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14, the fragment comprising eight contiguous amino acids of SEQ ID NO:14;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:13.
- 23. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:14;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:14, the fragment comprising eight contiguous amino acids of SEQ ID NO:14; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vj1\_1 deposited with the ATCC under accession number 98846; the protein being substantially free from other mammalian proteins.
- 24. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:15;
  - (b) the nucleotide sequence of SEQ ID NO:15 from nucleotide 62 to nucleotide 1057:
  - (c) the nucleotide sequence of SEQ ID NO:15 from nucleotide 659 to nucleotide 1057;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vl1\_1 deposited with the ATCC under accession number 98846;

(e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vl1\_1 deposited with the ATCC under accession number 98846;

- (f) the nucleotide sequence of a mature protein coding sequence of clone vl1\_1 deposited with the ATCC under accession number 98846;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vl1\_1 deposited with the ATCC under accession number 98846;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:16;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:16, the fragment comprising eight contiguous amino acids of SEQ ID NO:16;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:15.
- 25. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:16;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:16, the fragment comprising eight contiguous amino acids of SEQ ID NO:16; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vl1\_1 deposited with the ATCC under accession number 98846; the protein being substantially free from other mammalian proteins.
- 26. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:17;

(b) the nucleotide sequence of SEQ ID NO:17 from nucleotide 74 to nucleotide 529;

- (c) the nucleotide sequence of SEQ ID NO:17 from nucleotide 140 to nucleotide 529;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vk2\_1 deposited with the ATCC under accession number 98838;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vk2\_1 deposited with the ATCC under accession number 98838;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vk2\_1 deposited with the ATCC under accession number 98838;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vk2\_1 deposited with the ATCC under accession number 98838:
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:18;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:18, the fragment comprising eight contiguous amino acids of SEQ ID NO:18;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:17.
- 27. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:18;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:18, the fragment comprising eight contiguous amino acids of SEQ ID NO:18; and
  - (c) the amino acid sequence encoded by the cDNA insert of clone vk2\_1 deposited with the ATCC under accession number 98838;

the protein being substantially free from other mammalian proteins.

28. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:19;
- (b) the nucleotide sequence of SEQ ID NO:19 from nucleotide 174 to nucleotide 3170;
- (c) the nucleotide sequence of SEQ ID NO:19 from nucleotide 1098 to nucleotide 3170;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vb21\_1 deposited with the ATCC under accession number 98862;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vb21\_1 deposited with the ATCC under accession number 98862;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vb21\_1 deposited with the ATCC under accession number 98862;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vb21\_1 deposited with the ATCC under accession number 98862:
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:20;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20, the fragment comprising eight contiguous amino acids of SEQ ID NO:20;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:19.
- 29. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:20;
- (b) a fragment of the amino acid sequence of SEQ ID NO:20, the fragment comprising eight contiguous amino acids of SEQ ID NO:20; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vb21\_1 deposited with the ATCC under accession number 98862; the protein being substantially free from other mammalian proteins.
- 30. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:21;
  - (b) the nucleotide sequence of SEQ ID NO:21 from nucleotide 74 to nucleotide 1453;
  - (c) the nucleotide sequence of SEQ ID NO:21 from nucleotide 224 to nucleotide 1453;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vc35\_1 deposited with the ATCC under accession number 98862;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc35\_1 deposited with the ATCC under accession number 98862;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vc35\_1 deposited with the ATCC under accession number 98862;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc35\_1 deposited with the ATCC under accession number 98862;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:22;
  - (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22, the fragment comprising eight contiguous amino acids of SEQ ID NO:22;
  - (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
  - (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees

C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:21.

- 31. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:22;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:22, the fragment comprising eight contiguous amino acids of SEQ ID NO:22; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc35\_1 deposited with the ATCC under accession number 98862; the protein being substantially free from other mammalian proteins.
- 32. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:23;
  - (b) the nucleotide sequence of SEQ ID NO:23 from nucleotide 135 to nucleotide 368;
  - (c) the nucleotide sequence of SEQ ID NO:23 from nucleotide 243 to nucleotide 368;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vc36\_1 deposited with the ATCC under accession number 98862;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc36\_1 deposited with the ATCC under accession number 98862;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vc36\_1 deposited with the ATCC under accession number 98862;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc36\_1 deposited with the ATCC under accession number 98862;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:24;
  - (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24, the fragment comprising eight contiguous amino acids of SEQ ID NO:24;

(j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and

- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:23.
- 33. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:24;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:24, the fragment comprising eight contiguous amino acids of SEQ ID NO:24; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc36\_1 deposited with the ATCC under accession number 98862; the protein being substantially free from other mammalian proteins.
- 34. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:25;
  - (b) the nucleotide sequence of SEQ ID NO:25 from nucleotide 370 to nucleotide 1662;
  - (c) the nucleotide sequence of the full-length protein coding sequence of clone vc38\_1 deposited with the ATCC under accession number 98862;
  - (d) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc38\_1 deposited with the ATCC under accession number 98862;
  - (e) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:26;
  - (f) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26, the fragment comprising eight contiguous amino acids of SEQ ID NO:26;

(g) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d); and

- (h) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d), and that has a length that is at least 25% of the length of SEQ ID NO:25.
- 35. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:26;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:26, the fragment comprising eight contiguous amino acids of SEQ ID NO:26; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc38\_1 deposited with the ATCC under accession number 98862; the protein being substantially free from other mammalian proteins.
- 36. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:27;
  - (b) the nucleotide sequence of SEQ ID NO:27 from nucleotide 105 to nucleotide 365;
  - (c) the nucleotide sequence of SEQ ID NO:27 from nucleotide 147 to nucleotide 365;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vc39\_1 deposited with the ATCC under accession number 98862;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc39\_1 deposited with the ATCC under accession number 98862;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vc39\_1 deposited with the ATCC under accession number 98862;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc39\_1 deposited with the ATCC under accession number 98862;

 (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:28;

- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28, the fragment comprising eight contiguous amino acids of SEQ ID NO:28;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:27.
- 37. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:28;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:28, the fragment comprising eight contiguous amino acids of SEQ ID NO:28; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc39\_1 deposited with the ATCC under accession number 98862; the protein being substantially free from other mammalian proteins.
- 38. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:29;
  - (b) the nucleotide sequence of SEQ ID NO:29 from nucleotide 35 to nucleotide 1066;
  - (c) the nucleotide sequence of SEQ ID NO:29 from nucleotide 128 to nucleotide 1066;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vc40\_1 deposited with the ATCC under accession number 98862;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc40\_1 deposited with the ATCC under accession number 98862;

(f) the nucleotide sequence of a mature protein coding sequence of clone vc40\_1 deposited with the ATCC under accession number 98862;

- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc40\_1 deposited with the ATCC under accession number 98862;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:30;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30, the fragment comprising eight contiguous amino acids of SEQ ID NO:30;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:29.
- 39. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:30;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:30, the fragment comprising eight contiguous amino acids of SEQ ID NO:30; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc40\_1 deposited with the ATCC under accession number 98862; the protein being substantially free from other mammalian proteins.
- 40. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:31;
  - (b) the nucleotide sequence of SEQ ID NO:31 from nucleotide 38 to nucleotide 553;
  - (c) the nucleotide sequence of SEQ ID NO:31 from nucleotide 104 to nucleotide 553;

(d) the nucleotide sequence of the full-length protein coding sequence of clone vc46\_1 deposited with the ATCC under accession number 98862;

- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc46\_1 deposited with the ATCC under accession number 98862;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc46\_1 deposited with the ATCC under accession number 98862;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc46\_1 deposited with the ATCC under accession number 98862;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:32;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:32, the fragment comprising eight contiguous amino acids of SEQ ID NO:32;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:31.
- 41. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:32;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:32, the fragment comprising eight contiguous amino acids of SEQ ID NO:32; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc46\_1 deposited with the ATCC under accession number 98862; the protein being substantially free from other mammalian proteins.
- 42. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:33;
- (b) the nucleotide sequence of SEQ ID NO:33 from nucleotide 164 to nucleotide 2548;
- (c) the nucleotide sequence of SEQ ID NO:33 from nucleotide 242 to nucleotide 2548;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc49\_1 deposited with the ATCC under accession number 98862;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc49\_1 deposited with the ATCC under accession number 98862;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc49\_1 deposited with the ATCC under accession number 98862;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc49\_1 deposited with the ATCC under accession number 98862;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:34;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34, the fragment comprising eight contiguous amino acids of SEQ ID NO:34;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:33.
- 43. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:34;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:34, the fragment comprising eight contiguous amino acids of SEQ ID NO:34; and

(c) the amino acid sequence encoded by the cDNA insert of clone vc49\_1 deposited with the ATCC under accession number 98862; the protein being substantially free from other mammalian proteins.

- 44. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:35;
  - (b) the nucleotide sequence of SEQ ID NO:35 from nucleotide 150 to nucleotide 776;
  - (c) the nucleotide sequence of SEQ ID NO:35 from nucleotide 246 to nucleotide 776;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vc50\_1 deposited with the ATCC under accession number 98862;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc50\_1 deposited with the ATCC under accession number 98862;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vc50\_1 deposited with the ATCC under accession number 98862;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc50\_1 deposited with the ATCC under accession number 98862;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:36;
  - (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36, the fragment comprising eight contiguous amino acids of SEQ ID NO:36;
  - (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
  - (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:35.

45. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:36;
- (b) a fragment of the amino acid sequence of SEQ ID NO:36, the fragment comprising eight contiguous amino acids of SEQ ID NO:36; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc50\_1 deposited with the ATCC under accession number 98862; the protein being substantially free from other mammalian proteins.
- 46. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:37;
  - (b) the nucleotide sequence of SEQ ID NO:37 from nucleotide 139 to nucleotide 1308;
  - (c) the nucleotide sequence of SEQ ID NO:37 from nucleotide 211 to nucleotide 1308;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vc51\_1 deposited with the ATCC under accession number 98862;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc51\_1 deposited with the ATCC under accession number 98862;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vc51\_1 deposited with the ATCC under accession number 98862;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc51\_1 deposited with the ATCC under accession number 98862;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:38;
  - (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:38, the fragment comprising eight contiguous amino acids of SEQ ID NO:38;
  - (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and

(k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:37.

- 47. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:38;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:38, the fragment comprising eight contiguous amino acids of SEQ ID NO:38; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc51\_1 deposited with the ATCC under accession number 98862; the protein being substantially free from other mammalian proteins.
- 48. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:39;
  - (b) the nucleotide sequence of SEQ ID NO:39 from nucleotide 21 to nucleotide 1142:
  - (c) the nucleotide sequence of SEQ ID NO:39 from nucleotide 114 to nucleotide 1142;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vc52\_1 deposited with the ATCC under accession number 98862;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc52\_1 deposited with the ATCC under accession number 98862:
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vc52\_1 deposited with the ATCC under accession number 98862;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc52\_1 deposited with the ATCC under accession number 98862;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:40;

(i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40, the fragment comprising eight contiguous amino acids of SEQ ID NO:40;

- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:39.
- 49. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:40;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:40, the fragment comprising eight contiguous amino acids of SEQ ID NO:40; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc52\_1 deposited with the ATCC under accession number 98862; the protein being substantially free from other mammalian proteins.
- 50. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:41;
  - (b) the nucleotide sequence of SEQ ID NO:41 from nucleotide 13 to nucleotide 1416:
  - (c) the nucleotide sequence of SEQ ID NO:41 from nucleotide 346 to nucleotide 1416;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vc33\_1 deposited with the ATCC under accession number 98886;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc33\_1 deposited with the ATCC under accession number 98886;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vc33\_1 deposited with the ATCC under accession number 98886;

(g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc33\_1 deposited with the ATCC under accession number 98886;

- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:42;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:42, the fragment comprising eight contiguous amino acids of SEQ ID NO:42;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:41.
- 51. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:42;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:42, the fragment comprising eight contiguous amino acids of SEQ ID NO:42; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc33\_1 deposited with the ATCC under accession number 98886; the protein being substantially free from other mammalian proteins.
- 52. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:43;
  - (b) the nucleotide sequence of SEQ ID NO:43 from nucleotide 232 to nucleotide 1461;
  - (c) the nucleotide sequence of SEQ ID NO:43 from nucleotide 280 to nucleotide 1461;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vc34\_1 deposited with the ATCC under accession number 98886;

(e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc34\_1 deposited with the ATCC under accession number 98886;

- (f) the nucleotide sequence of a mature protein coding sequence of clone vc34\_1 deposited with the ATCC under accession number 98886;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc34\_1 deposited with the ATCC under accession number 98886;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:44;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44, the fragment comprising eight contiguous amino acids of SEQ ID NO:44;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:43.
- 53. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:44;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:44, the fragment comprising eight contiguous amino acids of SEQ ID NO:44; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc34\_1 deposited with the ATCC under accession number 98886; the protein being substantially free from other mammalian proteins.
- 54. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:45;

(b) the nucleotide sequence of SEQ ID NO:45 from nucleotide 1922 to nucleotide 2350;

- (c) the nucleotide sequence of SEQ ID NO:45 from nucleotide 2237 to nucleotide 2350;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc47\_1 deposited with the ATCC under accession number 98886;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc47\_1 deposited with the ATCC under accession number 98886;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc47\_1 deposited with the ATCC under accession number 98886;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc47\_1 deposited with the ATCC under accession number 98886;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:46;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46, the fragment comprising eight contiguous amino acids of SEQ ID NO:46;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:45.
- 55. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:46;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:46, the fragment comprising eight contiguous amino acids of SEQ ID NO:46; and
  - (c) the amino acid sequence encoded by the cDNA insert of clone vc47\_1 deposited with the ATCC under accession number 98886;

the protein being substantially free from other mammalian proteins.

56. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:47;
- (b) the nucleotide sequence of SEQ ID NO:47 from nucleotide 111 to nucleotide 1337;
- (c) the nucleotide sequence of SEQ ID NO:47 from nucleotide 246 to nucleotide 1337;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vc54\_1 deposited with the ATCC under accession number 98886;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc54\_1 deposited with the ATCC under accession number 98886;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vc54\_1 deposited with the ATCC under accession number 98886;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc54\_1 deposited with the ATCC under accession number 98886;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:48;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48, the fragment comprising eight contiguous amino acids of SEQ ID NO:48;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:47.
- 57. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:48;
- (b) a fragment of the amino acid sequence of SEQ ID NO:48, the fragment comprising eight contiguous amino acids of SEQ ID NO:48; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc54\_1 deposited with the ATCC under accession number 98886; the protein being substantially free from other mammalian proteins.
- 58. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:49;
  - (b) the nucleotide sequence of SEQ ID NO:49 from nucleotide 189 to nucleotide 1637;
  - (c) the nucleotide sequence of SEQ ID NO:49 from nucleotide 270 to nucleotide 1637;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vc57\_1 deposited with the ATCC under accession number 98886;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc57\_1 deposited with the ATCC under accession number 98886:
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vc57\_1 deposited with the ATCC under accession number 98886;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc57\_1 deposited with the ATCC under accession number 98886;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:50;
  - (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:50, the fragment comprising eight contiguous amino acids of SEQ ID NO:50;
  - (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
  - (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees

C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:49.

- 59. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:50;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:50, the fragment comprising eight contiguous amino acids of SEQ ID NO:50; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc57\_1 deposited with the ATCC under accession number 98886; the protein being substantially free from other mammalian proteins.
- 60. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:51;
  - (b) the nucleotide sequence of SEQ ID.NO:51 from nucleotide 15 to nucleotide 1934;
  - (c) the nucleotide sequence of SEQ ID NO:51 from nucleotide 1704 to nucleotide 1934;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vel3\_1 deposited with the ATCC under accession number 98886;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone ve13\_1 deposited with the ATCC under accession number 98886;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone ve13\_1 deposited with the ATCC under accession number 98886;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone ve13\_1 deposited with the ATCC under accession number 98886;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:52;
  - (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:52, the fragment comprising eight contiguous amino acids of SEQ ID NO:52;

(j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and

- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:51.
- 61. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:52;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:52, the fragment comprising eight contiguous amino acids of SEQ ID NO:52; and
- (c) the amino acid sequence encoded by the cDNA insert of clone ve13\_1 deposited with the ATCC under accession number 98886; the protein being substantially free from other mammalian proteins.
- 62. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:53;
  - (b) the nucleotide sequence of SEQ ID NO:53 from nucleotide 240 to nucleotide 503;
  - (c) the nucleotide sequence of SEQ ID NO:53 from nucleotide 318 to nucleotide 503;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone ve16\_1 deposited with the ATCC under accession number 98886;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone ve16\_1 deposited with the ATCC under accession number 98886:
  - (f) the nucleotide sequence of a mature protein coding sequence of clone ve16\_1 deposited with the ATCC under accession number 98886;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone ve16\_1 deposited with the ATCC under accession number 98886;

 (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:54;

- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:54, the fragment comprising eight contiguous amino acids of SEQ ID NO:54;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:53.
- 63. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:54;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:54, the fragment comprising eight contiguous amino acids of SEQ ID NO:54; and
- (c) the amino acid sequence encoded by the cDNA insert of clone ve16\_1 deposited with the ATCC under accession number 98886; the protein being substantially free from other mammalian proteins.
- 64. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:55;
  - (b) the nucleotide sequence of SEQ ID NO:55 from nucleotide 11 to nucleotide 1063;
  - (c) the nucleotide sequence of SEQ ID NO:55 from nucleotide 71 to nucleotide 1063;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vf3\_1 deposited with the ATCC under accession number 98886;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vf3\_1 deposited with the ATCC under accession number 98886:

(f) the nucleotide sequence of a mature protein coding sequence of clone vf3\_1 deposited with the ATCC under accession number 98886;

- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vf3\_1 deposited with the ATCC under accession number 98886:
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:56;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56, the fragment comprising eight contiguous amino acids of SEQ ID NO:56;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:55.
- 65. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:56;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:56, the fragment comprising eight contiguous amino acids of SEQ ID NO:56; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vf3\_1 deposited with the ATCC under accession number 98886; the protein being substantially free from other mammalian proteins.
- 66. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:57;
  - (b) the nucleotide sequence of SEQ ID NO:57 from nucleotide 542 to nucleotide 886;
  - (c) the nucleotide sequence of SEQ ID NO:57 from nucleotide 755 to nucleotide 886;

(d) the nucleotide sequence of the full-length protein coding sequence of clone vj2\_1 deposited with the ATCC under accession number 98886;

- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vj2\_1 deposited with the ATCC under accession number 98886:
- (f) the nucleotide sequence of a mature protein coding sequence of clone vj2\_1 deposited with the ATCC under accession number 98886;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vj2\_1 deposited with the ATCC under accession number 98886;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:58;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58, the fragment comprising eight contiguous amino acids of SEQ ID NO:58;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:57.
- 67. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:58;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:58, the fragment comprising eight contiguous amino acids of SEQ ID NO:58; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vj2\_1 deposited with the ATCC under accession number 98886; the protein being substantially free from other mammalian proteins.
- 68. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:59;
- (b) the nucleotide sequence of SEQ ID NO:59 from nucleotide 30 to nucleotide 344;
- (c) the nucleotide sequence of SEQ ID NO:59 from nucleotide 84 to nucleotide 344:
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vp7\_1 deposited with the ATCC under accession number 98886;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vp7\_1 deposited with the ATCC under accession number 98886;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vp7\_1 deposited with the ATCC under accession number 98886;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vp7\_1 deposited with the ATCC under accession number 98886;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:60;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:60, the fragment comprising eight contiguous amino acids of SEQ ID NO:60;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:59.
- 69. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:60;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:60, the fragment comprising eight contiguous amino acids of SEQ ID NO:60; and

(c) the amino acid sequence encoded by the cDNA insert of clone vp7\_1 deposited with the ATCC under accession number 98886; the protein being substantially free from other mammalian proteins.

- 70. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:61;
  - (b) the nucleotide sequence of SEQ ID NO:61 from nucleotide 23 to nucleotide 757;
  - (c) the nucleotide sequence of SEQ ID NO:61 from nucleotide 119 to nucleotide 757;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vp8\_1 deposited with the ATCC under accession number 98886;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vp8\_1 deposited with the ATCC under accession number 98886;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vp8\_1 deposited with the ATCC under accession number 98886;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vp8\_1 deposited with the ATCC under accession number 98886:
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:62;
  - (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:62, the fragment comprising eight contiguous amino acids of SEQ ID NO:62;
  - (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
  - (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:61.

71. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:62;
- (b) a fragment of the amino acid sequence of SEQ ID NO:62, the fragment comprising eight contiguous amino acids of SEQ ID NO:62; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vp8\_1 deposited with the ATCC under accession number 98886; the protein being substantially free from other mammalian proteins.
- 72. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:63;
  - (b) the nucleotide sequence of SEQ ID NO:63 from nucleotide 1048 to nucleotide 3726;
  - (c) the nucleotide sequence of the full-length protein coding sequence of clone vb22\_1 deposited with the ATCC under accession number 98933;
  - (d) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vb22\_1 deposited with the ATCC under accession number 98933;
  - (e) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:64;
  - (f) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64, the fragment comprising eight contiguous amino acids of SEQ ID NO:64;
  - (g) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d); and
  - (h) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d), and that has a length that is at least 25% of the length of SEQ ID NO:63.
- 73. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:64;
- (b) a fragment of the amino acid sequence of SEQ ID NO:64, the fragment comprising eight contiguous amino acids of SEQ ID NO:64; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vb22\_1 deposited with the ATCC under accession number 98933; the protein being substantially free from other mammalian proteins.
- 74. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:65;
  - (b) the nucleotide sequence of SEQ ID NO:65 from nucleotide 134 to nucleotide 667;
  - (c) the nucleotide sequence of SEQ ID NO:65 from nucleotide 191 to nucleotide 667;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vc48\_1 deposited with the ATCC under accession number 98933;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc48\_1 deposited with the ATCC under accession number 98933;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vc48\_1 deposited with the ATCC under accession number 98933;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc48\_1 deposited with the ATCC under accession number 98933;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:66;
  - (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:66, the fragment comprising eight contiguous amino acids of SEQ ID NO:66;
  - (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
  - (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees

C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:65.

- 75. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:66;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:66, the fragment comprising eight contiguous amino acids of SEQ ID NO:66; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc48\_1 deposited with the ATCC under accession number 98933; the protein being substantially free from other mammalian proteins.
- 76. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:67;
  - (b) the nucleotide sequence of SEQ ID NO:67 from nucleotide 65 to nucleotide 457;
  - (c) the nucleotide sequence of SEQ ID NO:67 from nucleotide 158 to nucleotide 457;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vp3\_1 deposited with the ATCC under accession number 98933;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vp3\_1 deposited with the ATCC under accession number 98933;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vp3\_1 deposited with the ATCC under accession number 98933;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vp3\_1 deposited with the ATCC under accession number 98933;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:68;
  - (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:68, the fragment comprising eight contiguous amino acids of SEQ ID NO:68;

(j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and

- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:67.
- 77. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:68;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:68, the fragment comprising eight contiguous amino acids of SEQ ID NO:68; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vp3\_1 deposited with the ATCC under accession number 98933; the protein being substantially free from other mammalian proteins.
- 78. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:69;
  - (b) the nucleotide sequence of SEQ ID NO:69 from nucleotide 29 to nucleotide 1387:
  - (c) the nucleotide sequence of SEQ ID NO:69 from nucleotide 113 to nucleotide 1387;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vc61\_1 deposited with the ATCC under accession number 207012;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vc61\_1 deposited with the ATCC under accession number 207012;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vc61\_1 deposited with the ATCC under accession number 207012;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vc61\_1 deposited with the ATCC under accession number 207012;

(h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:70;

- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:70, the fragment comprising eight contiguous amino acids of SEQ ID NO:70;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:69.
- 79. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:70;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:70, the fragment comprising eight contiguous amino acids of SEQ ID NO:70; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vc61\_1 deposited with the ATCC under accession number 207012; the protein being substantially free from other mammalian proteins.
- 80. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:71;
  - (b) the nucleotide sequence of SEQ ID NO:71 from nucleotide 44 to nucleotide 1513;
  - (c) the nucleotide sequence of SEQ ID NO:71 from nucleotide 92 to nucleotide 1513;
  - (d) the nucleotide sequence of SEQ ID NO:71 from nucleotide 1 to nucleotide 458;
  - (e) the nucleotide sequence of the full-length protein coding sequence of clone vp15\_1 deposited with the ATCC under accession number 207012;

(f) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vp15\_1 deposited with the ATCC under accession number 207012;

- (g) the nucleotide sequence of a mature protein coding sequence of clone vp15\_1 deposited with the ATCC under accession number 207012;
- (h) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vp15\_1 deposited with the ATCC under accession number 207012;
- (i) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:72;
- (j) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:72, the fragment comprising eight contiguous amino acids of SEQ ID NO:72;
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(h); and
- (I) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(h), and that has a length that is at least 25% of the length of SEQ ID NO:71.
- 81. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:72;
  - (b) the amino acid sequence of SEQ ID NO:72 from amino acid 1 to amino acid 139;
  - (c) a fragment of the amino acid sequence of SEQ ID NO:72, the fragment comprising eight contiguous amino acids of SEQ ID NO:72; and
- (d) the amino acid sequence encoded by the cDNA insert of clone vp15\_1 deposited with the ATCC under accession number 207012; the protein being substantially free from other mammalian proteins.
- 82. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:73;
- (b) the nucleotide sequence of SEQ ID NO:73 from nucleotide 348 to nucleotide 743;
- (c) the nucleotide sequence of SEQ ID NO:73 from nucleotide 414 to nucleotide 743;
- (d) the nucleotide sequence of the full-length protein coding sequence of clone vp17\_1 deposited with the ATCC under accession number 207012;
- (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vp17\_1 deposited with the ATCC under accession number 207012;
- (f) the nucleotide sequence of a mature protein coding sequence of clone vp17\_1 deposited with the ATCC under accession number 207012;
- (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vp17\_1 deposited with the ATCC under accession number 207012;
- (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:74;
- (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:74, the fragment comprising eight contiguous amino acids of SEQ ID NO:74;
- (j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:73.
- 83. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:74;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:74, the fragment comprising eight contiguous amino acids of SEQ ID NO:74; and

(c) the amino acid sequence encoded by the cDNA insert of clone vp17\_1 deposited with the ATCC under accession number 207012; the protein being substantially free from other mammalian proteins.

- 84. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:75;
  - (b) the nucleotide sequence of SEQ ID NO:75 from nucleotide 144 to nucleotide 461;
  - (c) the nucleotide sequence of the full-length protein coding sequence of clone vp19\_1 deposited with the ATCC under accession number 207012;
  - (d) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vp19\_1 deposited with the ATCC under accession number 207012;
  - (e) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:76;
  - (f) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:76, the fragment comprising eight contiguous amino acids of SEQ ID NO:76;
  - (g) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d); and
  - (h) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(d), and that has a length that is at least 25% of the length of SEQ ID NO:75.
- 85. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:76;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:76, the fragment comprising eight contiguous amino acids of SEQ ID NO:76; and
  - (c) the amino acid sequence encoded by the cDNA insert of clone vp19\_1 deposited with the ATCC under accession number 207012;

the protein being substantially free from other mammalian proteins.

86. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:77;
- (b) the nucleotide sequence of SEQ ID NO:77 from nucleotide 54 to nucleotide 368;
- (c) the nucleotide sequence of SEQ ID NO:77 from nucleotide 141 to nucleotide 368;
- (d) the nucleotide sequence of SEQ ID NO:77 from nucleotide 51 to nucleotide 332;
- (e) the nucleotide sequence of the full-length protein coding sequence of clone vq1\_1 deposited with the ATCC under accession number 207012;
- (f) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vq1\_1 deposited with the ATCC under accession number 207012;
- (g) the nucleotide sequence of a mature protein coding sequence of clone vq1\_1 deposited with the ATCC under accession number 207012;
- (h) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vq1\_1 deposited with the ATCC under accession number 207012;
- (i) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:78;
- (j) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:78, the fragment comprising eight contiguous amino acids of SEQ ID NO:78;
- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(h); and
- (l) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(h), and that has a length that is at least 25% of the length of SEQ ID NO:77.

87. A protein comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:78;
- (b) the amino acid sequence of SEQ ID NO:78 from amino acid 1 to amino acid 93;
- (c) a fragment of the amino acid sequence of SEQ ID NO:78, the fragment comprising eight contiguous amino acids of SEQ ID NO:78; and
- (d) the amino acid sequence encoded by the cDNA insert of clone vq1\_1 deposited with the ATCC under accession number 207012; the protein being substantially free from other mammalian proteins.
- 88. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) the nucleotide sequence of SEQ ID NO:79;
  - (b) the nucleotide sequence of SEQ ID NO:79 from nucleotide 2 to nucleotide 1018;
  - (c) the nucleotide sequence of SEQ ID NO:79 from nucleotide 53 to nucleotide 1018;
  - (d) the nucleotide sequence of the full-length protein coding sequence of clone vp14\_1 deposited with the ATCC under accession number 207011;
  - (e) a nucleotide sequence encoding the full-length protein encoded by the cDNA insert of clone vp14\_1 deposited with the ATCC under accession number 207011;
  - (f) the nucleotide sequence of a mature protein coding sequence of clone vp14\_1 deposited with the ATCC under accession number 207011;
  - (g) a nucleotide sequence encoding a mature protein encoded by the cDNA insert of clone vp14\_1 deposited with the ATCC under accession number 207011;
  - (h) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:80;
  - (i) a nucleotide sequence encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:80, the fragment comprising eight contiguous amino acids of SEQ ID NO:80;

(j) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 65 degrees C, or 4X SSC at 42 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g); and

- (k) the nucleotide sequence of a polynucleotide that hybridizes under conditions at least as stringent as 4X SSC at 50 degrees C, or 6X SSC at 40 degrees C with 50% formamide, to any one of the polynucleotides specified by (a)-(g), and that has a length that is at least 25% of the length of SEQ ID NO:79.
- 89. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:80;
  - (b) a fragment of the amino acid sequence of SEQ ID NO:80, the fragment comprising eight contiguous amino acids of SEQ ID NO:80; and
- (c) the amino acid sequence encoded by the cDNA insert of clone vp14\_1 deposited with the ATCC under accession number 207011; the protein being substantially free from other mammalian proteins.

Fig. 1A

WO 00/11015

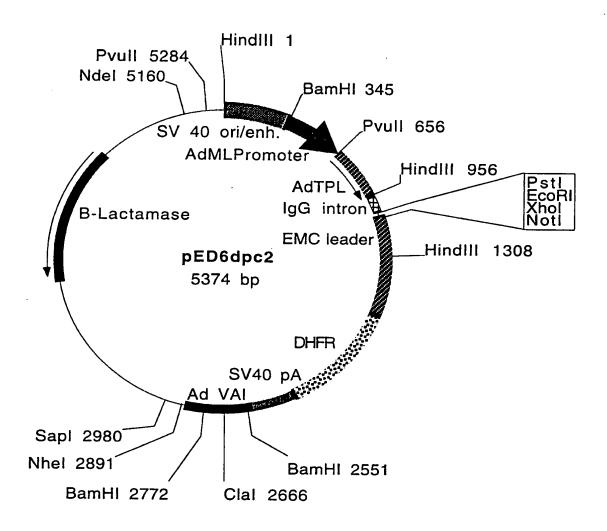
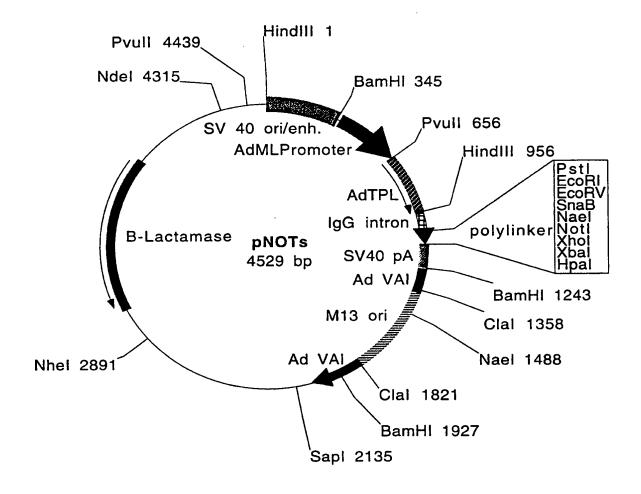


Fig. 1B



## SEQUENCE LISTING

```
<110> Valenzuela, Dario
      Yuan, Olive
      Hoffman, Heidi
      Hall, Jeff
      Rapiejko, Peter
<120> SECRETED PROTEINS AND POLYNUCLEOTIDES ENCODING THEM
<130> GI 6908X
<140>
<141>
<160> 132
<170> PatentIn Ver. 2.0
<210> 1
<211> 1738
<212> DNA
<213> Homo sapiens
<400> 1
acttagtgta gcaccaggga gccctagagc tggaggatat cgaatagatt aaattttgct 60
cgtctcttcc acaagcccta accatgggtc ttaaaaacag cagattctgg gagccttcca 120
tgetetetet eteteetett ttatetaett eceteecaaa tgagagagtg acagagaatt 180
gtttttttat aaatcgaagt ttcttaatag tatcaggttt tgatacgtca gtggtctaaa 240
atgctatagt gcaattacta gcagttactg cacggagtgc caccgtgcca atagaggact 300
gttgttttaa taagggaact cttagcccat ttcctccctc ccgccatctc taccettgct 360
caatgaaata tcatttaaat ttcttttaaa aaaaatcagt ttaattctta ctgtgtgccc 420
aacacgaagg cettttttga aagaaaaata gaatgttttg cetcaaagta gtecatataa 480
aatgtettga atagaagaaa aaactaccaa accaaaggtt actatttttg aaacategtg 540
tgttcattcc agcaaggcag aagactgcac cttctttcca gtgacatgct gtgtcatttt 600
ttttaagtcc tcttaatttt tagacacatt tttggtttat gttttaacaa tgtatgccta 660
accagtcate ttgtetgeac caatgcaaag gtttetgaga ggagtattet etatecetgt 720
ggatatgaag acactggcat ttcatctatt tttccctttc ctttttaaag gatttaactt 780
tggaatette caaaggaagt ttggecaatg ccagateece aggaatttgg ggggtttet 840
ttetttteaa etgaaattgt atetgattee taetgtteat gttagtgate atetaateae 900
agagccaaac acttttctcc cctgtgtgga aaagtaggta tgctttacaa taaaatctgt 960
cttttctggt agaaacctga gccactgaaa ataaaagaga caactagaag cacagtagag 1020
teccagactg agatetacet ttgagagget ttgaaagtaa teectggggt ttggattatt 1080
ttcacaaggg ttatgccgtt ttattcaagt ttgttgctcc gttttgcacc tctgcaataa 1140
aagcaaaatg acaaccagta cataaggggt tagcttgaca aagtagactt ccttgtgtta 1200
atttttaagt tttttttcc ttaactatat ctgtctacag gcagatacag atagttgtat 1260
gaaaatctgc ttgcctgtaa aatttgcatt tataaatgtg ttgccgatgg atcacttggg 1320
cctgtacaca taccaattag cgtgaccact tccatcttaa aaacaaacct aaaaaacaaa 1380
atttattata tatatata tatatatata aaggactgtg ggttgtatac aaactattgc 1440
aaacacttgt gcaaatctgt cttgatataa aggaaaagca aaatctgtat aacattatta 1500
ctacttgaat gcctctgtga ctgattttt ttttcatttt aaatataaac ttttttgtga 1560
aaagtatget caatgttttt ttteeettte eccatteeet tgtaaataca ttttgtteta 1620
tgtgacttgg tttggaaata gttaactggt actgtaattt gcattaaata aaaagtaggt 1680
<210> 2
<211> 84
<212> PRT
<213> Homo sapiens
```

```
<400> 2
Met Gln Arg Phe Leu Arg Gly Val Phe Ser Ile Pro Val Asp Met Lys
                                   10
Thr Leu Ala Phe His Leu Phe Phe Pro Phe Leu Phe Lys Gly Phe Asn
             20
                                25
Phe Gly Ile Phe Gln Arg Lys Phe Gly Gln Cys Gln Ile Pro Arg Asn
Leu Gly Gly Phe Leu Ser Phe Gln Leu Lys Leu Tyr Leu Ile Pro Thr
Val His Val Ser Asp His Leu Ile Thr Glu Pro Asn Thr Phe Leu Pro
 65
                    70
                                       75
Cys Val Glu Lys
<210> 3
<211> 2198
<212> DNA
<213> Homo sapiens
<400> 3
gctctgtgga ttctggccag gccgggttcg gcggttgctg tgagagcggg cttcccaaca 60
ccatgccgtc cgccttctct gtcagctctt tccccgtcag catcccagcc gtgctcacgc 120
agacggactg gactgagece tggetcatgg ggetggeeae ettecaegeg etetgegtge 180
tecteacetg ettgteetee egaagetaca gaetacagat egggeacttt etgtgtetag 240
tcatcttagt ctactgtgct gaatacatca atgaggcggc tgcgatgaac tggagattat 300
tttcgaaata ccagtatttc gactccaggg ggatgttcat ttctatagta ttttcagccc 360
cactgctggt gaatgccatg atcattgtgg ttatgtgggt atggaagact ttgaatgtga 420
actgaggggc agcagctgct tggagtttgc gtccttcccg tccacccagt gcagctccca 540
gtgctgcagt gtgcgtggcg tgggcatcct tccagctgac tcatggtttg aaaaaccgtt 600
gttttattta aatatccaca gtggtagggc acacactgaa gttggctttt cagccagcac 660
tgaatgtate eateaggaea tgegtettea ggtgeetgat etttgtagte aggetgtggg 720
gtaactagta ctaattataa atataaaata cacaatataa aatatgaaac tcaataataa 840
acagtgccac ctgtacatgg gcaccatgcc ctcctcctcg tgctgtgttt tctagtgcat 900
gccacagttc gcagtagagg gtgttttcac cttccaagac atggggcaaa gtttggagac 960
acctggttgt cactggaggg ggtggtgctc ctggcttctc ctgtggagcc cggggtgatg 1020
cataaaatcc tgtgtgcctg ggtcagccgc atcacagaca atgacttgac atgaaatgtc 1080
agctgtgctg gggcagagag accttggaag gaagctcttg gaaaatacgt tgtatctcag 1140
tttgatgaac caattcacaa gaggctaggc cctctctagc aaagttatgg gctgctttac 1200
tgaaaacaga atggaageee tgaagteaac acteeatgga gaagegtgte ttteetaatg 1260
tectggtgtt etgttgattt aggtgettgg gaacacaatg etcecagtte tgttaggaca 1320
ggcatactgt tactttgcaa tatccacttt ataaaatagc tcctgcccag tggctcttgg 1380
ttcctgtcaa atgtggacct gtagtttaag aatgacaggt ggttagagac ccagatattt 1440
aaaaataggt gttcaataag ggaatactga ttgtgcattg tatctggata gcatgcctaa 1500
ttgtgcattt ctgaaagtta ccaattcaaa atgtaattgg aacagttatc tttgattaga 1560
caageetggg aagagaatgt tgaggtgcag ageteaceag ceaagtteat geeeteteg 1620
ggcctttgtg gctgagaagt gggacagaaa gatgattaag gtaatgtgtc ctccctgtag 1680
cattgtccag ggccgttgtg tagatatttg acttcactga cagaaaagaa accagggagt 1740
ttgtagagac tgtgcatttt tagtataaca ttttcaccat ctgatatggt ttggctttgt 1800
gtccccaccc aaattgcatc tcaaattgta atccccatgt gtcaagggag ggacctgatg 1860
ggaggtgatg ggatcatggg ggtggtttcc cctatgttgt tatcataata gagagggagt 1920
teteacaaga tetgetegtt ttaaagacag cagttteece tgetgteact gtetetetee 1980
tgctgccttg tgaagaaggt gcttgtttct ccctctgcca tgattgtaag tttcccgagg 2040
```

cctccccggc catgtggaac tgagtcaatt aaacttcttg tttataaagt aaaaaaaaa 2100

```
aaaaaaaaa aaaaaaaaa aaaaaaaaa
                                                                2198
<210> 4
<211> 140
<212> PRT
<213> Homo sapiens
<400> 4
Met Pro Ser Ala Phe Ser Val Ser Ser Phe Pro Val Ser Ile Pro Ala
Val Leu Thr Gln Thr Asp Trp Thr Glu Pro Trp Leu Met Gly Leu Ala
            20
Thr Phe His Ala Leu Cys Val Leu Leu Thr Cys Leu Ser Ser Arg Ser
Tyr Arg Leu Gln Ile Gly His Phe Leu Cys Leu Val Ile Leu Val Tyr
Cys Ala Glu Tyr Ile Asn Glu Ala Ala Ala Met Asn Trp Arg Leu Phe
Ser Lys Tyr Gln Tyr Phe Asp Ser Arg Gly Met Phe Ile Ser Ile Val
Phe Ser Ala Pro Leu Leu Val Asn Ala Met Ile Ile Val Val Met Trp
                               105
                                                  110
Val Trp Lys Thr Leu Asn Val Met Thr Asp Leu Lys Asn Ala Gln Glu
                          120
Arg Arg Lys Glu Lys Lys Arg Arg Arg Lys Glu Asp
                      135
<210> 5
<211> 2229
<212> DNA
<213> Homo sapiens
<400> 5
ggagccgggc aaccagtgga aggagcctgg gagaggccag gcctccccgg actgctagcc 60
tgetttteet ggggteeetg gageeggagg aagaaceagg atgttgetge etgeagaage 120
tcagctcagg aagacttcca ggaacctgag gaggagctgc cactaacagc catattccc 180
aatggagact gtgatgacct tggaaggggg tcaaaagcct gtgatggagt cgtacacact 240
cctgctgagc ccaccggaga ctcaagatga aggctggacc cttgcgctgt ccctggctct 300
aacctacaga ctggggcctg gctccgtctt actggccccc aggtctccat ggagactgca 360
gaaacccccg cctgctggag gcctgccaca ctcacagtta ccagctagac agtggggctt 420
actaagacaa gcaggaccta aaacagtgtc tcccctggga acctactccc cacccagcat 480
ttgctaagtc tgatcacagg gaggttattt tgtctctctg tctcggtttc tctgagccac 540
tgagacagat ggctgtccgc tttgaggctc tgcagagctg tggcacccca tggtgtgtct 600
gcagtgttct gggcacatgc atgggcaccc atcgttgaga gtgcagctgg gaagaactct 660
gaaccagaag teateagage tgaggeatgg cettgaacat gteacteagt etetgggget 720
tctgtttcac aaatgcatga gggggccacc agcccagtgg ctttaaacca ggggcaggtt 780
gtccctccag gcagcattgg aaatgtgtgt gtgttgaggg ggtcacagtg actgtggggg 840
cacccctggc atctagtggg catcccacaa tgtgcagaac agtctctgac agcaaagaat 900
tggtccattc aatgccaatt gtagtacctt tgagacattc tggctgagcc aatgccttct 960
```

```
ccctgtcaga gtcccccaga gcagagaggg tcaggcttcc ctggaccttg gctcccagag 1020
caagccaaaa taaagactac actgttgcct tggggggcttg tcgggccagg gccaagacgg 1080
tctgcgtgct gcagggccag gacagaaata gccacacatg ccggtgagaa caaagagcct 1140
ctttctttct catgttgaca tcgactttct gtgccaagtc ctttgggtat aaggatgcta 1200
gggaatteet ataggeacea aacagaagga aagetagggg ettggactae tgggtatagg 1260
acttgeteta geteteaggt cetageceaa geteaatgea aacacagece eteegggete 1320
totgtttctg tgaggttctg gaatcccttc ctctgtgtcc gtgagtctga cagaatcgat 1380
gatgttccct tagagctggg aaatccatgt gtttattcac ggagggaact caccattacc 1440
tecettgtet tetttgeetg eettggagaa atccagagte tteggaatgg caaaggeage 1500
tcctggattt ccctggaggg gaggcactag ctgagggaag tagctccctt cattcatgat 1560
gcacagttta cgcagcagac acacaactgc gcctactatt tgctcggtgc cctgcaaggt 1620
gctgcctaac tttgatttgt tatttcagct ctctccagga tagtgccaaa tggtgcaatg 1680
ggaaacctgt tttgctgggg ggctctagat cactggctcc agaactcccg gctgccaggg 1740
tagcccctac ccccagcccc ttgctcctgg acagcagtgg gtctcacctt tagcctctgc 1800
ccccagttct ggtctgaccc aacagagggg ctctatgata ttaagaaggg gcccttcctg 1860
ctctgtgcct caacctattc tccataatag ggagtctaat cctattcctt ccctgcctga 1920
tgaggatggt gtgaggatga ggaggacggc atctcatttg gggctttttg gcagtgggcc 1980
tcattttaat cctgcagggc tgcctgccag tggatctatc cagctgcttc cttgtagcca 2040
agaatgagtt caatgaattg tgattcactg attttattga ttttgtttta aaacagggag 2100
actggtattt ttgaagctgc tatcattttc tatttcttta ttaatttctt tgtaatcatc 2160
aaaaaaaa
<210> 6
<211> 111
<212> PRT
<213> Homo sapiens
<400> 6
Met Leu Gly Asn Ser Tyr Arg His Gln Thr Glu Gly Lys Leu Gly Ala
Trp Thr Thr Gly Tyr Arg Thr Cys Ser Ser Ser Gln Val Leu Ala Gln
Ala Gln Cys Lys His Ser Pro Ser Gly Leu Ser Val Ser Val Arg Phe
Trp Asn Pro Phe Leu Cys Val Arg Glu Ser Asp Arg Ile Asp Asp Val
Pro Leu Glu Leu Gly Asn Pro Cys Val Tyr Ser Arg Arg Glu Leu Thr
                    70
Ile Thr Ser Leu Val Phe Phe Ala Cys Leu Gly Glu Ile Gln Ser Leu
Arg Asn Gly Lys Gly Ser Ser Trp Ile Ser Leu Glu Gly Arg His
           100
                              105
<210> 7
<211> 915
<212> DNA
<213> Homo sapiens
<400> 7
cagececete ecetacteae catggtattt eteettgaat teetettet tgttttettt 120
cctggttgtg tgaaccagtt gctgctgtca tacccctggc agggccaggg gacctctctt 180
```

```
tggtcatttc tgtcctttca ctggctgctg ccccaggaag actcctctag gctctccatc 240
tttcccttga gagctggctc cccaccccaa cctgctcagg caccaccgag gatctaggtc 300
tctggctccc catacctgga cccacatggg tgggtgcctg ttgcatgttt aagagagagg 360
qqctqtqaqq tqacaqqqca ctagggcctt cactecttte teeetteea teetttett 420
accagtgcca cccatgtccc tagctcccgg gtattggggc tgaggctctg gggcctgtct 480
ccctgccage gtgagggcaa gaccccagag ccttagctga gcaagcccag aggggcagcg 540
tggcccctcc ctcccctttt cctgccccgt cccatgcctc agcttgctgc ttgtgccagt 600
tgcctgtttc gcttcagtgt ttgattctag cacttacatg tgtcctcccc accaagccct 660
ctatctcctt ctaatccttc aacccctggc cccctcccca taacagtgac ttttccaggg 720
aggaagaggc agcaggagct gttggccttg gtttgcacag agcgggtagg gctgtaggga 780
aagegggtga getgttgtge tgetgggeet eeetttggee etegetteee accetacgat 840
gtatgaaatg tatgtacaga ccagagatgt ttatacagcc gataaagatg gaaaaaaaaa 900
aaaaaaaaa aaaaa
                                                                915
<210> 8
<211> 71
<212> PRT
<213> Homo sapiens
<400> 8
Met Val Phe Leu Leu Glu Phe Leu Phe Leu Val Phe Pro Gly Cys
                 5
Val Asn Gln Leu Leu Ser Tyr Pro Trp Gln Gly Gln Gly Thr Ser
Leu Trp Ser Phe Leu Ser Phe His Trp Leu Leu Pro Gln Glu Asp Ser
Ser Arg Leu Ser Ile Phe Pro Leu Arg Ala Gly Ser Pro Pro Gln Pro
Ala Gln Ala Pro Pro Arg Ile
                    70
<210> 9
<211> 1100
<212> DNA
<213> Homo sapiens
tgacccccaa gacggaagag gatggccgcg gcggctctga ggagattttg gtcccggcgc 60
cgcgcagagg cggggcgcc cgctgtgtat gtgggtctgc tggggcggcg ggcggcctgc 120
ttcacgctgg cgcccagcga gggtgccttc gaggaggcgc tgctggaggc gtcggggacc 180
ctcctgctgc tggcgccggc cacccgcaac cgcgggtcct ggacgtgggc ttcgtgggtc 240
gctggtgggt gctgggggcc tggatgcgcg actgcgacat caacgacgac gàattcctgc 300
acctgccggc gcatttgcgg gtggtcgggc cccagcagct gcattccgag accaacgagc 360
ggctcttcga tgagaagtac aagcctgtcg tgctcaccga cgatcaggtg gaccaggcgc 420
tgtgggagga gcaggtcttg cagaaggaga agaaggacag gctcgccctg agccaggccc 480
actcgctggt gcaggcggag gccccgagat gaaaccctga ggcccccgag tcctggcaaa 540
ctgcttgcct ggggtggtgc agttctgagt gtgcctcacc tgcagaacag ctgagacaga 600
tgatgtgcaa agtgttttct cactggattt gcacaagttt ggggagcctt tctgccccc 660
gtetttgtte tttattaget gaagetaatt eagageeace tgggteeggg agttggggae 720
agcagaacga cttgacacat gttcatcact ggcagagctg gtcatgagcc ttttatataa 780
gcctttttca tcgggcctca gaggccctcc ttaaggaggt accacattgg tcagctgact 840
tgcaaactct tctaaggcca cttagatttt ctttttcaag tttgggttgt ggcctggcat 900
ggtgatgtct gtaatcccag cagtttgcaa actgaggcaa gagaatcgct tgaggccagg 960
agtttgaggc cagctagagt gacatagcaa gactccgatg ctacaaaaaa gaataataat 1020
```

aaaaaaaaaa aaaaaaaaaa 1100 <210> 10 <211> 149 <212> PRT <213> Homo sapiens <400> 10 Met Ala Ala Ala Leu Arg Arg Phe Trp Ser Arg Arg Ala Glu 5 Ala Gly Arg Ala Ala Val Tyr Val Gly Leu Leu Gly Gly Ala Ala Ala Cys Phe Thr Leu Ala Pro Ser Glu Gly Ala Phe Glu Glu Ala Leu Leu Glu Ala Ser Gly Thr Leu Leu Leu Leu Ala Pro Ala Thr Arg Asn Arg 55 Gly Ser Trp Thr Trp Ala Ser Trp Val Ala Gly Gly Cys Trp Gly Pro Gly Cys Ala Thr Ala Thr Ser Thr Thr Thr Asn Ser Cys Thr Cys Arg 90 Arg Ile Cys Gly Trp Ser Gly Pro Ser Ser Cys Ile Pro Arg Pro Thr Ser Gly Ser Ser Met Arg Ser Thr Ser Leu Ser Cys Ser Pro Thr Ile 120 Arg Trp Thr Arg Arg Cys Gly Arg Ser Arg Ser Cys Arg Arg Arg Arg 135 140 Arg Thr Gly Ser Pro <210> 11 <211> 2010 <212> DNA <213> Homo sapiens <400> 11 tggtgagctg cagagaagag gaggttggtg tggagcacag gcagcaccga gcctgccccg 60 tgagctgagg gcctgcagtc tgcggctgga atcaggatag acaccaaggc aggacccca 120 gagatgetga agcetetttg gaaageagea gtggeeecea catggeeatg etceatgeeg 180 eccegeegee egtgggaeag agaggetgge aegttgeagg teetgggage getggetgtg 240 etgtggetgg geteegtgge tettatetge etectgtgge aagtgeeeeg teeteecace 300 tggggccagg tgcagcccaa ggacgtgccc aggtcctggg agcatggctc cagcccagct 360 tgggagcccc tggaagcaga ggccaggcag cagagggact cctgccagct tgtccttgtg 420 gaaagcatee eecaggaeet gecatetgea geeggeagee eetetgeeea geetetggge 480 caggcctggc tgcagctgct ggacactgcc caggagagcg tccacgtggc ttcatactac 540 tggtccctca cagggcctga catcggggtc aacgactcgt cttcccagct gggagaggct 600 cttctgcaga agctgcagca gctgctgggc aggaacattt ccctggctgt ggccaccagc 660

agcccgacac tggccaggac atccaccgac ctgcaggttc tggctgcccg aggtgcccat 720 gtacgacagg tgcccatggg gcggctcacc aggggtgttt tgcactccaa attctgggtt 780 gtggatggac ggcacatata catgggcagt gccaacatgg actggcggtc tctgacgcag 840 gtgaaggagc ttggcgctgt catctataac tgcagccacc tggcccaaga cctggagaag 900

```
accttccaga cctactgggt actgggggtg cccaaggctg tcctccccaa aacctggcct 960
cagaacttct catctcactt caaccgtttc cagcccttcc acggcctctt tgatggggtg 1020
cccaccactg cctacttctc agcgtcgcca ccagcactct gtccccaggg ccgcaccgg 1080
gacctggagg cgctgctggc ggtgatgggg agcgcccagg agttcatcta tgcctccgtg 1140
atggagtatt tecceaceae gegetteage caeeeeega ggtaetggee ggtgetggae 1200
aacgcgctgc gggcggcagc cttcggcaag ggcgtgcgcg tgcgcctgct ggtcggctgc 1260
ggactcaaca cggaccccac catgttcccc tacctgcggt ccctgcaggc gctcagcaac 1320
cccgcggcca acgtctctgt ggacgtgaaa gtcttcatcg tgccggtggg gaaccattcc 1380
aacatcccat tcagcagggt gaaccacagc aagttcatgg tcacggagaa ggcagcctac 1440
ataggcacct ccaactggtc ggaggattac ttcagcagca cggcgggggt gggcttggtg 1500
gtcacccaga gccctggcgc gcagcccgcg ggggccacgg tgcaggagca gctgcggcag 1560
ctctttgagc gggactggag ttcgcgctac gccgtcggcc tggacggaca ggctccgggc 1620
caggactgcg tttggcaggg ctgagggggg cctctttttc tctcggcgac cccgcccgc 1680
acgegeette ceetetgace eeggeetggg etteageege tteeteege aageageeeg 1740
ggtccgcact gcgccaggag ccgcctgcga ccgcccgggc gtcgcaaacc gcccgcctgc 1800
tetetgattt cegagtecag cececetga gececacete etecagggag cectecagga 1860
agcecettee etgacteetg geecacagge caggeetaaa aaaaactegt ggettaaaaa 1920
aaaaaaaaa aaaaaaaaa aaaaaaaaaa
<210> 12
<211> 506
<212> PRT
<213> Homo sapiens
<400> 12
Met Leu Lys Pro Leu Trp Lys Ala Ala Val Ala Pro Thr Trp Pro Cys
Ser Met Pro Pro Arg Arg Pro Trp Asp Arg Glu Ala Gly Thr Leu Gln
Val Leu Gly Ala Leu Ala Val Leu Trp Leu Gly Ser Val Ala Leu Ile
Cys Leu Leu Trp Gln Val Pro Arg Pro Pro Thr Trp Gly Gln Val Gln
Pro Lys Asp Val Pro Arg Ser Trp Glu His Gly Ser Ser Pro Ala Trp
Glu Pro Leu Glu Ala Glu Ala Arg Gln Gln Arg Asp Ser Cys Gln Leu
Val Leu Val Glu Ser Ile Pro Gln Asp Leu Pro Ser Ala Ala Gly Ser
Pro Ser Ala Gln Pro Leu Gly Gln Ala Trp Leu Gln Leu Leu Asp Thr
                           120
Ala Gln Glu Ser Val His Val Ala Ser Tyr Tyr Trp Ser Leu Thr Gly
                       135
Pro Asp Ile Gly Val Asn Asp Ser Ser Ser Gln Leu Gly Glu Ala Leu
                                      155
Leu Gln Lys Leu Gln Gln Leu Leu Gly Arg Asn Ile Ser Leu Ala Val
               165
                                  170
```

Ala Thr Ser Ser Pro Thr Leu Ala Arg Thr Ser Thr Asp Leu Gln Val

180 185 190 Leu Ala Ala Arg Gly Ala His Val Arg Gln Val Pro Met Gly Arg Leu Thr Arg Gly Val Leu His Ser Lys Phe Trp Val Val Asp Gly Arg His 215 Ile Tyr Met Gly Ser Ala Asn Met Asp Trp Arg Ser Leu Thr Gln Val 230 235 Lys Glu Leu Gly Ala Val Ile Tyr Asn Cys Ser His Leu Ala Gln Asp Leu Glu Lys Thr Phe Gln Thr Tyr Trp Val Leu Gly Val Pro Lys Ala 265 Val Leu Pro Lys Thr Trp Pro Gln Asn Phe Ser Ser His Phe Asn Arg 280 Phe Gln Pro Phe His Gly Leu Phe Asp Gly Val Pro Thr Thr Ala Tyr 295 Phe Ser Ala Ser Pro Pro Ala Leu Cys Pro Gln Gly Arg Thr Arg Asp Leu Glu Ala Leu Leu Ala Val Met Gly Ser Ala Gln Glu Phe Ile Tyr 325 330 Ala Ser Val Met Glu Tyr Phe Pro Thr Thr Arg Phe Ser His Pro Pro 345 Arg Tyr Trp Pro Val Leu Asp Asn Ala Leu Arg Ala Ala Ala Phe Gly 360 Lys Gly Val Arg Val Arg Leu Leu Val Gly Cys Gly Leu Asn Thr Asp 375 Pro Thr Met Phe Pro Tyr Leu Arg Ser Leu Gln Ala Leu Ser Asn Pro 390 395 Ala Ala Asn Val Ser Val Asp Val Lys Val Phe Ile Val Pro Val Gly 405 Asn His Ser Asn Ile Pro Phe Ser Arg Val Asn His Ser Lys Phe Met 425 Val Thr Glu Lys Ala Ala Tyr Ile Gly Thr Ser Asn Trp Ser Glu Asp Tyr Phe Ser Ser Thr Ala Gly Val Gly Leu Val Val Thr Gln Ser Pro 455 Gly Ala Gln Pro Ala Gly Ala Thr Val Gln Glu Gln Leu Arg Gln Leu 470 Phe Glu Arg Asp Trp Ser Ser Arg Tyr Ala Val Gly Leu Asp Gly Gln 485 490

8

Ala Pro Gly Gln Asp Cys Val Trp Gln Gly

500 505

<210> 13 <211> 2830 <212> DNA

<213> Homo sapiens

<400> 13 ggcagaggca tgctcatggt gctccttccc cagcagcaat cctatgctcc ccttccaggt 60 cttctcttcc ttctttcct cagccagctg gctgctggta agagaggtct ggcgagagtg 120 tgtcccagta gctgctgcta tggatggaac ggaggggca ggacgtaggc tggaggagtc 180 tgtcttcccg gcatctttac gagatcgctg ctgcaggacc ttaatcatag catctttctc 240 tatgattttg gcatggagat ttttaatagt gtattccatg tcctgacacc ttctgttggc 300 ctgcaccacc tectectect ettgccagat gtgggeetee agegagetet eteegtaget 360 gccattccgt gagtggttga tgatcgtggt gtccctctca gctgctgcag tggctgcggc 420 attcatggca aagtgtcgga tggtgctctc ctccaggtac ttctgctccc actttgtcat 480 gteggeetee agggeeagga teegeteete etteteeege acaagtteea ggagggetgg 540 ggcattgtat tccggcatgt tggctggctg gccatttcca tgtttctgct gggttctcag 600 tgcatccage teteteteca gecaagteeg cagteteege tecatetgtt etegettete 660 acatgcagac tgcagctggg tcagggcctg ctgcagcttc tcaactttct caacatatgc 720 ttgcttctct cgtaactcct cttccagctt gatgaccctg gcctgggcgt tgctcaaagc 780 ctggtccagg atctcgatgt gtctccgatg gtcctcactt gcagtccgca ctgctgctaa 840 ctccatttct aatttctcct tttccttcaa gaattctttg ttctgggaag cataatgccc 900 ctctgcagct ttgtcttcat gcccttcgta ttccctgctg gatagttgcc tgttagcagt 960 ctctagtcga tctcggaggt ctctgttgaa atcatgaagt cttctaatct cgccttccaa 1020 tttgtttctc atggccttgt ccagcgattc tcgcttggtg gtagacttga ccagactttc 1080 ataggettee gaaattetet gaagttettt tteaaaettg tggagettgt eggeattgte 1140 gtagtaaccc tgaagttcct ggtgaagcac ccggttctcc tctgttaata tctccaccat 1200 ttgctgggct cgctccacaa tcgcaaaggc atctggacca agctgctggc tggggggaggc 1260 ggcaggcggg ggctgtggag cacccagggc catcgggagt ggaagcggca gggagacaga 1320 gtgcagtggc ccgctggcgg aagaggtctg ggaggacatg gggctgtgct gctgcatggt 1380 tgatgggaac ggaagttggc atgggcggct cgttacccca tactcagggg gtggctggta 1440 ecgeaggacg gecacatetg tteteacagg etgaggagea gggtaggget tgaccatete 1500 gtggagcatc ccggggtgct ggtcaccata aaaaagtccg tgctcctggg tcttgctgac 1560 tggggacatc atttgcttgg tcttgaaggg gtactcaggt ggaggacccc gagggtccag 1620 cactttacct gcaggctggg caggggaggg cccccctcct actttgaagc cctttccatt 1680 ccccgagccg ggaaggtgtt gcttggcccc attcctctcc agggacagct gcatgattct 1740 ctcgctgagc gagcggacgt ggccctgctt cagttccttc agcgcctcgt ccttatgcgc 1800 ctgtccactg ttggcacggt tcacagtggg cctccctca gttcgggact tctgactggt 1860 gececetgee atgragtaac catggeceae egececetge tgetgttget getgetgetg 1920 ecceetgaag aactgegaet gtgetttgge etectegtaa gtgggeagtt eetegttgtt 1980 ctgctgaggc tgcgtggacc ggacctgttt ctccatcacc gtattgtcca cctggtgttc 2040 ttgaccctgc ggttcttggc gtgctgactg gtagaccatt tgtgggtctt cttgagtgag 2100 gttttccgtg gaagaaaagt tgtttgtagg atgggctggt cctgcactcc ctgtggcctg 2160 gtgctgaatg gccagcaagt tcatgttctc ggttggggtg ccataccgca gttgttcctg 2220 gatcagccgc tgcaatactg ttccagctgc cgcatcctcg gaacctctca tttccacctc 2280 tgagatcctc aggaagtttg gggagtggaa gttacaaaga ggatcttcaa caactttttc 2340 cctgatgcta ctggttgcct ccaccgtcaa agcagatgtt tcatgcctcc cagaatagag 2400 ctgaaagtct ggggaaaagt aggtggagtc ttctagaacc tggacaggac tactggggct 2460 ataacaagca gaaggggacc ctaactcgtc tgggctgtag gatgcgggcg aggcttccac 2520 aaactcactg tctgggggag aagaaaagca gaaaacaact cgaatcgcta ccattcagga 2580 cgaacccgcc aagcaccagc tcaagcgcag gtccccggga aaagcgcggg cttctctctc 2640 ccagcgctca gaatccctga gccggaggcc ccgcgggatt cagaccgcca gatccccagg 2700 gagtgacaaa tcgccgcaga aacttggggg acaactcggc cctggcaccg cgcggcttcc 2760 aggegeggte aggegegee caacttteee egegtgeeae eeeggeggete eeeeggeegg 2820

<210> 14 <211> 171

gcgctgggcc

<212> PRT <213> Homo sapiens <400> 14 Met Ile Val Val Ser Leu Ser Ala Ala Ala Val Ala Ala Ala Phe Met Ala Lys Cys Arg Met Val Leu Ser Ser Arg Tyr Phe Cys Ser His Phe 25 Val Met Ser Ala Ser Arg Ala Arg Ile Arg Ser Ser Phe Ser Arg Thr 40 Ser Ser Arg Arg Ala Gly Ala Leu Tyr Ser Gly Met Leu Ala Gly Trp Pro Phe Pro Cys Phe Cys Trp Val Leu Ser Ala Ser Ser Ser Leu Ser Ser Gln Val Arg Ser Leu Arg Ser Ile Cys Ser Arg Phe Ser His Ala 85 Asp Cys Ser Trp Val Arg Ala Cys Cys Ser Phe Ser Thr Phe Ser Thr 100 Tyr Ala Cys Phe Ser Arg Asn Ser Ser Ser Ser Leu Met Thr Leu Ala Trp Ala Leu Leu Lys Ala Trp Ser Arg Ile Ser Met Cys Leu Arg Trp 135 Ser Ser Leu Ala Val Arg Thr Ala Ala Asn Ser Ile Ser Asn Phe Ser 150 Phe Ser Phe Lys Asn Ser Leu Phe Trp Glu Ala 165 <210> 15 <211> 2000 <212> DNA <213> Homo sapiens <400> 15 gcagaagetg taegggetee aggetgacat taccateage etggaeggeg tgeeetteet 60 catgcatgac accaecetge ggegeaceae caaegtggag gaggagttee eggagetgge 120 ccgcaggeet geetecatge ttaactggae caccetgeag agaeteaaeg etggccagtg 180 gttcctgaag actgacccct tctggacagc cagctccctg tcaccctccg accacagaga 240 ggcccagaac cagtccatct gcagcctggc agagctcctg gagctggcca agggcaatgc 300 cacactgctg ctcaacetgc gtgacccgcc ccgggagcac ccctaccgca gcagttttat 360 caacgtgact ctggaggccg tgctgcactc cggcttcccc cagcaccagg tcatgtggct 420 gectageagg cagaggeece tggtgeggaa ggtggeteee ggettecaac agacateagg 480 ctccaaggag gcagtcgcca gcctgcggag aggccacatc cagcggctga acctgcgcta 540 cactcaggtg tecegecagg agetcaggga ctacgegtee tggaacetga gtgtgaacet 600 ctacacagte aacgeaccgt ggetettete cetgetgtgg tgtgcggggg teccatecgt 660 cacctetgae aacteecaea ecetgteeca ggtgeettee eceetetgga teatgeecee 720

ggacgagtac tgtctcatgt gggtcactgc cgacctggtc tccttcaccc tcatcgtggg 780 catcttcgtg ctccagaagt ggcgcctggg tggcatacgg agctacaacc ctgagcagat 840 catgctgagt gctgcggtcc gccggaccag ccgggacgtc agcatcatga aggagaagct 900 tattttctca gagatcagcg atggtgtaga ggtctccgat gtgctctccg tatgttcaga 960

```
caacagttat gacacatatg ccaacagcac cgccacccct gtgggccccc gagggggtgg 1020
cagecacace aagaceetca tagageggag tgggegttag etgaagacat gtetgteeca 1080
cetgtacetg acacagaage tggggageet aggagagetg gtggaagtgt gtctgaacte 1140
ggagtgetet gggageggge tecacageet cettgtggge tecageeect tgteageege 1200
agcetetett gagggggaet ecetgteece tgaggeecag etgggeeagg actecateet 1260
ttcagatgcc cctgcaggcc tggggctcct tctgggaagt atggggccta gggcttggtc 1320
cccctcttct gaggccctct cctgtatccc gacctggaag ctttgatggg tcatgggcca 1380
tgccataccc cctgtggcaa tggagtgtgt ggatgctcac ctgtgccatc tgtcctcctg 1440
tetgtgecag gaggeacetg agttetetge tgttateetg ceceaaggge etgggeegag 1500
cetetacetg aageaactet getetteetg teagteteaa ageacaagga ggtteageec 1560
aggaggaage cagetgeaat gtggagacae gteeteetee ceaacceace teatgeeace 1620
gccaaccccc tgccccagga gcgggcctga gccacgtccc ctaggagcag ctggagatgg 1680
ccaaaagagt gagctcaagg actactggga tcccaatgcc agtgtccagc agacctcaag 1740
gcagaagggt cacctaaccc aggagtccac agactgatgt gacctcaggt teccacatca 1800
gtggccacag ggcagggccc acctggtaga agtgttctgg atatggccag ggtgggtgtg 1860
tggctaagtg ggcctgaaca gagggaacct agggcccttg gcccaatgtg attaaaggct 1920
aaaaaaaaa aaaaaaaaaa
<210> 16
<211> 332
<212> PRT
<213> Homo sapiens
<400> 16
Met His Asp Thr Thr Leu Arg Arg Thr Thr Asn Val Glu Glu Phe
Pro Glu Leu Ala Arg Arg Pro Ala Ser Met Leu Asn Trp Thr Thr Leu
                                25
Gln Arg Leu Asn Ala Gly Gln Trp Phe Leu Lys Thr Asp Pro Phe Trp
Thr Ala Ser Ser Leu Ser Pro Ser Asp His Arg Glu Ala Gln Asn Gln
Ser Ile Cys Ser Leu Ala Glu Leu Leu Glu Leu Ala Lys Gly Asn Ala
                    70
Thr Leu Leu Asn Leu Arg Asp Pro Pro Arg Glu His Pro Tyr Arg
Ser Ser Phe Ile Asn Val Thr Leu Glu Ala Val Leu His Ser Gly Phe
           100
Pro Gln His Gln Val Met Trp Leu Pro Ser Arg Gln Arg Pro Leu Val
Arg Lys Val Ala Pro Gly Phe Gln Gln Thr Ser Gly Ser Lys Glu Ala
Val Ala Ser Leu Arg Arg Gly His Ile Gln Arg Leu Asn Leu Arg Tyr
                   150
                                      155
Thr Gln Val Ser Arg Gln Glu Leu Arg Asp Tyr Ala Ser Trp Asn Leu
                                  170
Ser Val Asn Leu Tyr Thr Val Asn Ala Pro Trp Leu Phe Ser Leu Leu
                              185
```

```
Trp Cys Ala Gly Val Pro Ser Val Thr Ser Asp Asn Ser His Thr Leu
                             200
Ser Gln Val Pro Ser Pro Leu Trp Ile Met Pro Pro Asp Glu Tyr Cys
                      215
Leu Met Trp Val Thr Ala Asp Leu Val Ser Phe Thr Leu Ile Val Gly
                    230
Ile Phe Val Leu Gln Lys Trp Arg Leu Gly Gly Ile Arg Ser Tyr Asn
Pro Glu Gln Ile Met Leu Ser Ala Ala Val Arg Arg Thr Ser Arg Asp
            260
                                265
Val Ser Ile Met Lys Glu Lys Leu Ile Phe Ser Glu Ile Ser Asp Gly
Val Glu Val Ser Asp Val Leu Ser Val Cys Ser Asp Asn Ser Tyr Asp
                        295
Thr Tyr Ala Asn Ser Thr Ala Thr Pro Val Gly Pro Arg Gly Gly Gly
                    310
                                        315
Ser His Thr Lys Thr Leu Ile Glu Arg Ser Gly Arg
<210> 17
<211> 1170
<212> DNA
<213> Homo sapiens
<400> 17
aagtttgtte eeegagtteg gageetagga geeeceegeg getgeggege aggtgeete 60
ggcctgagtc gggatggagc tgcctgctgt gaacctgaag gtgattctcc taggtcactg 120
gctgctgaca acctggggct gcattgtatt ctcaggctcc tatgcctggg ccaacttcac 180
catcetggce ttgggcgtgt gggctgtggc tcagcgggac tccatcgacg ccataagcat 240
gtttctgggt ggcttgctgg ccaccatctt cctggacatc gtgcacatca gcatcttcta 300
eccgegggte agecteaegg acaegggeeg etttggegtg ggeatggeea tecteagett 360
gctgctcaag ccgctctcct gctgcttcgt ctaccacatg taccgggagc gcgggggttt 420
ccttgggtct tctcaggacc gtagtgccta ccagacgatt gactcagcag aggcgcccgc 480
agatecettt geagteceag agggeaggag teaagatgee egagggtaet gaageeagee 540
acgetgegee eggeeetgee eegggeette etegtgeetg ggaggtegtt etagggatge 600
tectgacete egtetettgg acctaagatg gaatgtgtee eeageteagg gattgeetga 660
accaagagge caggageece catgggeege ceagtaceat geacacteet gteeegaact 720
ecctgaggee teccetecet teagggeace cactggttee caggetggaa ecagggtete 780
tetttacete etaceccatg gtggcaccac agaggecete agecgagtee tgeetgagtg 840
ttgcaagete aggeetttaa ggaetgetga tgccccetca ggeeteecee aagtttgetg 900
ggetttggtg gaageeetga gagetteagg teetgeteag eeegaggage agtetgacat 960
gggagtgagg ccctgtcctt ctcactgcct ggtcacatgg tgcctaggga tgcagggctg 1020
gaggecagag gtgtcagcaa cactgtgacc caccacaacc tecagectec ettttcagag 1080
cacagcatta aagtttgggg aattctgtaa aaaaaaaaa aaaaaaaaa aaaaaaaaa 1140
aaaaaaaaa aaaaaaaaaaaaaaaa
                                                                  1170
<210> 18
<211> 152
<212> PRT
```

<213> Homo sapiens

<400> 18 Met Glu Leu Pro Ala Val Asn Leu Lys Val Ile Leu Leu Gly His Trp 1 5 10 Leu Leu Thr Thr Trp Gly Cys Ile Val Phe Ser Gly Ser Tyr Ala Trp Ala Asn Phe Thr Ile Leu Ala Leu Gly Val Trp Ala Val Ala Gln Arg Asp Ser Ile Asp Ala Ile Ser Met Phe Leu Gly Gly Leu Leu Ala Thr Ile Phe Leu Asp Ile Val His Ile Ser Ile Phe Tyr Pro Arg Val Ser Leu Thr Asp Thr Gly Arg Phe Gly Val Gly Met Ala Ile Leu Ser Leu 85 90 Leu Leu Lys Pro Leu Ser Cys Cys Phe Val Tyr His Met Tyr Arg Glu 105 Arg Gly Gly Phe Leu Gly Ser Ser Gln Asp Arg Ser Ala Tyr Gln Thr 120 Ile Asp Ser Ala Glu Ala Pro Ala Asp Pro Phe Ala Val Pro Glu Gly 135 Arg Ser Gln Asp Ala Arg Gly Tyr 145 150 <210> 19 <211> 4144 <212> DNA <213> Homo sapiens <400> 19 ctccttgggc aggtgaggat aacagccctg tggcgagctg gtcctgagca tctgagtgag 60 cagtgatgcg gagaaatgac cttggtggga ggggacgtcc acagacgtga cccggacgtc 120 gggacaggtg gatctggggt caaggggagt gtttagaata cttgttggca tccatgacgc 180 cetteetgee teaggaggag tgteagaact acgtgegagt cetgategte geeggeegga 300 aggtgttcat gtgtggaacc aatgcetttt ceeccatgtg caccageaga caggtgggga 360 accteageeg gactattgag aagateaatg gtgtggeeeg etgeeeetat gacceaegee 420 acaactccac agctgtcatc tecteccagg gggageteta tgcagecacg gtcatcgact 480 tetcaggteg ggaccetgec atetacegea geetgggeag tgggecaceg ettegeactg 540 cccaatataa ctccaagtgg cttaatgagc caaacttcgt ggcagcctat gatattgggc 600 tgtttgcata cttcttcctg cgggagaacg cagtggagca cgactgtgga cgcaccgtgt 660 actotogogt ggcccgcgtg tgcaagaatg acgtgggggg ccgattootg ctggaggaca 720 catggaccac attcatgaag geoeggetea actgeteeeg eeeggegag gteeeettet 780 actataacga gctgcagagt gccttccact tgccggagca ggacctcatc tatggagttt 840 tcacaaccaa cgtaaacagc attgcggctt ctgctgtctg cgccttcaac ctcagtgcta 900 teteccagge tttcaatgge ceattteget accaggagaa ceccaggget geetggetee 960 ccatagccaa ccccatcccc aatttccagt gtggcaccct gcctgagacc ggtcccaacg 1020 agaacctgac ggagcgcagc ctgcaggacg cgcagcgcct cttcctgatg agcgaggccg 1080 tgcagccggt gacacccgag ccctgtgtca cccaggacag cgtgcgcttc tcacacctcg 1140 tggtggacct ggtgcaggct aaagacacgc tctaccatgt actctacatt ggcaccgagt 1200

cgggcaccat cctgaaggcg ctgtccacgg cgagccgcag cctccacggc tgctacctgg 1260

```
aggagetgea egtgetgeec eeegggegee gegageeett gegeageetg egeateetge 1320
acagegeeeg egegetette gtggggetga gagaeggegt eetgegggte eeactggaga 1380
ggtgcgccgc ctaccgcagc cagggggcat gcctgggggc ccgggacccg tactgtggct 1440
gggacgggaa gcagcaacgt tgcagcacac tcgaggacag ctccaacatg agcctctgga 1500
cccagaacat caccgcctgt cctgtgcgga atgtgacacg ggatgggggc ttcggcccat 1560
ggtcaccatg gcaaccatgt gagcacttgg atggggacaa ctcaggctct tgcctgtgtc 1620
gagetegate etgtgattee cetegaceee getgtggggg cettgactge etggggeeag 1680
ccatccacat cgccaactgc tccaggaatg gggcgtggac cccgtggtca tcgtgggcgc 1740
tgtgcagcac gtcctgtggc atcggcttcc aggtccgcca gcgaagttgc agcaaccctg 1800
ctccccgcca cgggggccgc atctgcgtgg gcaagagccg ggaggaacgg ttctgtaatg 1860
agaacacgcc ttgcccggtg cccatcttct gggcttcctg gggctcctgg agcaagtgca 1920
gcagcaactg tggagggggc atgcagtcgc ggcgtcgggc ctgcgagaac ggcaactcct 1980
geetgggetg eggegtggag ttcaagaegt geaaceeega gggetgeeee gaagtgegge 2040
gcaacacccc ctggacgccg tggctgcccg tgaacgtgac gcagggcggg gcacggcagg 2100
agcageggtt cegetteace tgeegegge ceettgeaga eeegeacgge etgeagtteg 2160
gcaggagaag gaccgagacg aggacctgtc ccgcggacgg ctccggctcc tgcgacaccg 2220
acgeeetggt ggaggacete etgegeageg ggagcacete eeegeacaeg gtgagegggg 2280
gctgggccgc ctggggcccg tggtcgtcct gctcccggga ctgcgagctg ggcttccgcg 2340
teegeaagag aacgtgeact aacceggage eeegeaacgg gggeetgeee tgegtgggeg 2400
atgctgccga gtaccaggac tgcaaccccc aggcttgccc agttcggggt gcttggtcct 2460
gctggacctc atggtctcca tgctcagctt cctgtggtgg gggtcactat caacgcaccc 2520
gttcctgcac cagccccgca ccctccccag gtgaggacat ctgtctcggg ctgcacacgg 2580
aggaggcact atgtgccaca caggcctgcc cagaaggctg gtcgccctgg tctgagtgga 2640
gtaagtgcac tgacgacgga gcccagagcc gaagccggca ctgtgaggag ctcctcccag 2700
ggtccagcgc ctgtgctgga aacagcagcc agagccgccc ctgcccctac agcgagattc 2760
ccgtcatcct gccagcctcc agcatggagg aggccaccgg ctgtgcaggg ttcaatctca 2820
tecacttggt ggccacgggc atctcctgct tettgggete tgggeteetg accetageag 2880
tgtacctgtc ttgccagcac tgccagcgtc agtcccagga gtccacactg gtccatcctg 2940
ccaccccaa ccatttgcac tacaagggcg gaggcacccc gaagaatgaa aagtacacac 3000
ccatggaatt caagaccetg aacaagaata acttgateee tgatgacaga gecaacttet 3060
acceattgea geagaceaat gtgtacaega etaettaeta eccaageeee etgaacaaac 3120
acagetteeg geeegaggee teacetggae aaeggtgett eeceaaeage tgataeegee 3180
gtcctgggga cttgggcttc ttgccttcat aaggcacaga gcagatggag atgggacagt 3240
ggagccagtt tggttttctc cctctgcact aggccaagaa cttgctgcct tgcctgtggg 3300
gggtcccatc cggcttcaga gagctctggc tggcattgac catgggggaa agggctggtt 3360
tcaggctgac atatggccgc aggtccagtt cagcccaggt ctctcatggt tatcttccaa 3420
cccactgtca cgctgacact atgctgccat gcctgggctg tggacctact gggcatttga 3480
ggaattggag aatggagatg gcaagagggc aggcttttaa gtttgggttg gagacaactt 3540
cctgtggccc ccacaagctg agtctggcct tctccagctg gccccaaaaa aggcctttgc 3600
tacatectga ttatetetga aagtaateaa teaagtgget eeagtagete tggatttet 3660
gccagggctg ggccattgtg gtgctgcccc agtatgacat gggaccaagg ccagcgcagg 3720
ttatccacct ctgcctggaa gtctatactc tacccagggc atccctctgg tcagaggcag 3780
tgagtactgg gaactggagg ctgacctgtg cttagaagtc ctttaatctg ggctggtaca 3840
ggcctcagcc ttgccctcaa tgcacgaaag gtggcccagg agagaggatc aatgccatag 3900
gaggcagaag tetggeetet gtgeetetat ggagactate ttecagttge tgeteaacag 3960
agttgttggc tgagacctgc ttgggagtct ctgctggccc ttcatctgtt caggaacaca 4020
cacacacaca cactcacaca cgcacacaca atcacaattt gctacagcaa caaaaaagac 4080
aaaa
                                                                 4144
<210> 20
<211> 999
<212> PRT
<213> Homo sapiens
<400> 20
Met Thr Gln Trp Cys Glu Arg Glu Ile Ser Ser Ile Ala Pro Gly Glu
                 5
                                    10
```

Leu Cys Cys Leu Leu Ser Phe Leu Pro Gln Glu Glu Cys Gln Asn

20 25 30

Tyr Val Arg Val Leu Ile Val Ala Gly Arg Lys Val Phe Met Cys Gly

- Thr Asn Ala Phe Ser Pro Met Cys Thr Ser Arg Gln Val Gly Asn Leu 50 60
- Ser Arg Thr Ile Glu Lys Ile Asn Gly Val Ala Arg Cys Pro Tyr Asp 65 70 75 80
- Pro Arg His Asn Ser Thr Ala Val Ile Ser Ser Gln Gly Glu Leu Tyr 85 90 95
- Ala Ala Thr Val Ile Asp Phe Ser Gly Arg Asp Pro Ala Ile Tyr Arg 100 105 110
- Ser Leu Gly Ser Gly Pro Pro Leu Arg Thr Ala Gln Tyr Asn Ser Lys 115 120 125
- Trp Leu Asn Glu Pro Asn Phe Val Ala Ala Tyr Asp Ile Gly Leu Phe 130 135 140
- Ala Tyr Phe Phe Leu Arg Glu Asn Ala Val Glu His Asp Cys Gly Arg 145 150 155 160
- Thr Val Tyr Ser Arg Val Ala Arg Val Cys Lys Asn Asp Val Gly Gly 165 170 175
- Arg Phe Leu Leu Glu Asp Thr Trp Thr Thr Phe Met Lys Ala Arg Leu 180 185 190
- Asn Cys Ser Arg Pro Gly Glu Val Pro Phe Tyr Tyr Asn Glu Leu Gln 195 200 205
- Ser Ala Phe His Leu Pro Glu Gln Asp Leu Ile Tyr Gly Val Phe Thr 210 215 220
- Thr Asn Val Asn Ser Ile Ala Ala Ser Ala Val Cys Ala Phe Asn Leu 225 230 235 240
- Ser Ala Ile Ser Gln Ala Phe Asn Gly Pro Phe Arg Tyr Gln Glu Asn 245 250 255
- Pro Arg Ala Ala Trp Leu Pro Ile Ala Asn Pro Ile Pro Asn Phe Gln 260 265 270
- Cys Gly Thr Leu Pro Glu Thr Gly Pro Asn Glu Asn Leu Thr Glu Arg 275 280 285
- Ser Leu Gln Asp Ala Gln Arg Leu Phe Leu Met Ser Glu Ala Val Gln 290 295 300
- Pro Val Thr Pro Glu Pro Cys Val Thr Gln Asp Ser Val Arg Phe Ser 305 310 315 320
- His Leu Val Val Asp Leu Val Gln Ala Lys Asp Thr Leu Tyr His Val
- Leu Tyr Ile Gly Thr Glu Ser Gly Thr Ile Leu Lys Ala Leu Ser Thr

340 345 350 Ala Ser Arg Ser Leu His Gly Cys Tyr Leu Glu Glu Leu His Val Leu 355 360 365 Pro Pro Gly Arg Arg Glu Pro Leu Arg Ser Leu Arg Ile Leu His Ser 375 Ala Arg Ala Leu Phe Val Gly Leu Arg Asp Gly Val Leu Arg Val Pro Leu Glu Arg Cys Ala Ala Tyr Arg Ser Gln Gly Ala Cys Leu Gly Ala 410 Arg Asp Pro Tyr Cys Gly Trp Asp Gly Lys Gln Gln Arg Cys Ser Thr Leu Glu Asp Ser Ser Asn Met Ser Leu Trp Thr Gln Asn Ile Thr Ala 440 Cys Pro Val Arg Asn Val Thr Arg Asp Gly Gly Phe Gly Pro Trp Ser 455 Pro Trp Gln Pro Cys Glu His Leu Asp Gly Asp Asn Ser Gly Ser Cys 470 Leu Cys Arg Ala Arg Ser Cys Asp Ser Pro Arg Pro Arg Cys Gly Gly 490 Leu Asp Cys Leu Gly Pro Ala Ile His Ile Ala Asn Cys Ser Arg Asn 505 Gly Ala Trp Thr Pro Trp Ser Ser Trp Ala Leu Cys Ser Thr Ser Cys Gly Ile Gly Phe Gln Val Arg Gln Arg Ser Cys Ser Asn Pro Ala Pro Arg His Gly Gly Arg Ile Cys Val Gly Lys Ser Arg Glu Glu Arg Phe Cys Asn Glu Asn Thr Pro Cys Pro Val Pro Ile Phe Trp Ala Ser Trp Gly Ser Trp Ser Lys Cys Ser Ser Asn Cys Gly Gly Met Gln Ser 585 Arg Arg Ala Cys Glu Asn Gly Asn Ser Cys Leu Gly Cys Gly Val 600 Glu Phe Lys Thr Cys Asn Pro Glu Gly Cys Pro Glu Val Arg Arg Asn 615 Thr Pro Trp Thr Pro Trp Leu Pro Val Asn Val Thr Gln Gly Gly Ala 630 635 Arg Gln Glu Gln Arg Phe Arg Phe Thr Cys Arg Ala Pro Leu Ala Asp 645 650 Pro His Gly Leu Gln Phe Gly Arg Arg Thr Glu Thr Arg Thr Cys

660 665 Pro Ala Asp Gly Ser Gly Ser Cys Asp Thr Asp Ala Leu Val Glu Asp 680 Leu Leu Arg Ser Gly Ser Thr Ser Pro His Thr Val Ser Gly Gly Trp Ala Ala Trp Gly Pro Trp Ser Ser Cys Ser Arg Asp Cys Glu Leu Gly Phe Arg Val Arg Lys Arg Thr Cys Thr Asn Pro Glu Pro Arg Asn Gly 730 Gly Leu Pro Cys Val Gly Asp Ala Ala Glu Tyr Gln Asp Cys Asn Pro Gln Ala Cys Pro Val Arg Gly Ala Trp Ser Cys Trp Thr Ser Trp Ser 760 Pro Cys Ser Ala Ser Cys Gly Gly Gly His Tyr Gln Arg Thr Arg Ser 775 Cys Thr Ser Pro Ala Pro Ser Pro Gly Glu Asp Ile Cys Leu Gly Leu 790 His Thr Glu Glu Ala Leu Cys Ala Thr Gln Ala Cys Pro Glu Gly Trp Ser Pro Trp Ser Glu Trp Ser Lys Cys Thr Asp Asp Gly Ala Gln Ser 825 Arg Ser Arg His Cys Glu Glu Leu Leu Pro Gly Ser Ser Ala Cys Ala 840 Gly Asn Ser Ser Gln Ser Arg Pro Cys Pro Tyr Ser Glu Ile Pro Val 855 Ile Leu Pro Ala Ser Ser Met Glu Glu Ala Thr Gly Cys Ala Gly Phe Asn Leu Ile His Leu Val Ala Thr Gly Ile Ser Cys Phe Leu Gly Ser 885 890 Gly Leu Leu Thr Leu Ala Val Tyr Leu Ser Cys Gln His Cys Gln Arg 905 Gln Ser Gln Glu Ser Thr Leu Val His Pro Ala Thr Pro Asn His Leu 920 His Tyr Lys Gly Gly Gly Thr Pro Lys Asn Glu Lys Tyr Thr Pro Met 935 Glu Phe Lys Thr Leu Asn Lys Asn Asn Leu Ile Pro Asp Asp Arg Ala 950 Asn Phe Tyr Pro Leu Gln Gln Thr Asn Val Tyr Thr Thr Thr Tyr Tyr

Pro Ser Pro Leu Asn Lys His Ser Phe Arg Pro Glu Ala Ser Pro Gly

980 985 990 Gln Arg Cys Phe Pro Asn Ser 995 <210> 21 <211> 2820 <212> DNA <213> Homo sapiens <400> 21 agaatgggag ctgtcagtta tcattcagga caaaggcaat cctcagctac ataccaaagt 60 ccttctgaag tgcatgatct ttgaatatgc agagtcggtg acaagtacag caatgacttc 120 agtaagccag gcatccttgg atgtctccat gataataatt atttccttag gagcaatttg 180 tgcagtgttg ctggttatta tggtgctatt tgcaactagg tgtaaccgcg agaagaaaga 240 cactagatec tataactgca gggtggccga atcaacttac cagcaccacc caaaaaggcc 300 atcccggcag attcacaaag gggacatcac attggtgcct accataaatg gcactctgcc 360 catcagatet catcacagat egtetecate tteatetect acettagaaa gagggeagat 420 gggcagccgg cagagtcaca acagtcacca gtcactcaac agtttggtga caatctcatc 480 aaaccacgtg ccagagaatt tctcattaga actcacccac gccactcctg ctgttgaggt 540 ctctcagctt ctttcaatgc ttcaccaggg gcaatatcag ccaagaccaa gttttcgagg 600

aaacaaatat tccaggagct acagatatgc ccttcaagac atggacaaat ttagcttgaa 660 agacagtggc cgtggtgaca gtgaggcagg agacagtgat tatgatttgg ggcgagattc 720 tccaatagat aggctgttgg gtgaaggatt cagcgacctg tttctcacag atggaagaat 780 tccagcagct atgagactct gcacggagga gtgcagggtc ctgggacact ctgaccagtg 840 ctggatgcca ccactgccct caccgtcttc tgattatagg agtaacatgt tcattccagg 900 ggaagaattc ccaacgcaac cccagcagca gcatccacat cagagtcttg aggatgacgc 960 tcagcctgca gattccggtg aaaagaagaa gagtttttcc acctttggaa aggactcccc 1020 aaacgatgag gacactgggg ataccagcac atcatctctg ctctcggaaa tgagcagtgt 1080 gttccagcgt ctcttaccgc cttccctgga cacctattct gaatgcagtg aggtggatcg 1140 gtccaactcc ctggagcgca ggaagggacc cttgccagcc aaaactgtgg gttacccaca 1200 gggggtagcg gcatgggcag ccagtacgca ttttcaaaat cccaccacca actgtgggcc 1260 gccacttgga actcactcca gtgtgcagcc ttcttcaaaa tggctgccag ccatggagga 1320 gatccctgaa aattatgagg aagatgattt tgacaatgtg ctcaaccacc tcaatgatgg 1380 gaaacacgaa ctcatggatg ccagtgaact ggtggcagag attaacaaac tgcttcaaga 1440 tgtccgccag agctaggaga ttttagcgaa gcatttttgt ttccatgtat atggaaatag 1500 ggaacaacaa caacaacaaa aaaccctgaa agaactggca ttgccaaata gttgcattta 1560 tcataaatgt gtctgtgtat attgaatatt aaatactgta ttttcgtatg tacacaatgc 1620

tttaacaaac aaattttatt tttttactc catgacagac atgttttcc tagtcgtgta 1740 gaaactagcc actgttcaaa tctgatacac tattcaacca caaagtgtaa aggcactgct 1800 tagattagtt ttgttgggga agaattatta tgttgtatga acaaccccac tgaagcatta 1860 tacaattctt aattccatta agtgatccca cttttttca ataacttttt agaaattaag 1920 aatcattaaa attgttaagc tattttattg ttattttctc tactttctac tagccccaat 1980 agttgaactc ttataggaaa atcgaaagat aaagtgaaag tttatttcag gactgagaaa 2040 tatcttgaag gttattatt agatgactat ctcaaatgaa ctttttatag acaatgatga 2100 aaacagaatt aaagtcaatg tttcctgact cccaggcccc tactattcca ggccatcaca 2160 ctggcctgtt ccggagaata tttctctcac aatattatta tctacttata attatggtaa 2220 acaataaatt ttattccatc cttgtagtat ggaacatgct ccaaggaaat ggaatctgtc 2280 ctttaaatgg ataacagtat gtgttctaat ggcataaaat attactggat aaaacagtt 2400 tgaacctccc ctttcctcc acaatacttg acaattctaa tcttttggaa caatctatt 2400 tgaacctccc ctttcctcc acaatacttg acaattctaa tcttttggaa tattgtctt 2460 tgaacctccc ctttcctcc acaatacttg acaattctaat ctttttggaa tattgtcatt 2460 ttttttata

aagtgtgatt attttaatct gtattttaaa aatacatttg taccttatat ttatgtgtaa 1680

<210> 22 <211> 460

<212> PRT

<213> Homo sapiens

<400> 22

Met Ile Phe Glu Tyr Ala Glu Ser Val Thr Ser Thr Ala Met Thr Ser 1 5 10 15

Val Ser Gln Ala Ser Leu Asp Val Ser Met Ile Ile Ile Ser Leu 20 25 30

Gly Ala Ile Cys Ala Val Leu Leu Val Ile Met Val Leu Phe Ala Thr 35 40 45

Arg Cys Asn Arg Glu Lys Lys Asp Thr Arg Ser Tyr Asn Cys Arg Val 50 60

Ala Glu Ser Thr Tyr Gln His His Pro Lys Arg Pro Ser Arg Gln Ile
65 70 75 80

His Lys Gly Asp Ile Thr Leu Val Pro Thr Ile Asn Gly Thr Leu Pro 85 90 95

Ile Arg Ser His His Arg Ser Ser Pro Ser Ser Ser Pro Thr Leu Glu 100 105 110

Arg Gly Gln Met Gly Ser Arg Gln Ser His Asn Ser His Gln Ser Leu 115 120 125

Asn Ser Leu Val Thr Ile Ser Ser Asn His Val Pro Glu Asn Phe Ser 130 140

Leu Glu Leu Thr His Ala Thr Pro Ala Val Glu Val Ser Gln Leu Leu 145 150 155 160

Ser Met Leu His Gln Gly Gln Tyr Gln Pro Arg Pro Ser Phe Arg Gly 165 170 175

Asn Lys Tyr Ser Arg Ser Tyr Arg Tyr Ala Leu Gln Asp Met Asp Lys 180 185 190

Phe Ser Leu Lys Asp Ser Gly Arg Gly Asp Ser Glu Ala Gly Asp Ser 195 200 205

Asp Tyr Asp Leu Gly Arg Asp Ser Pro Ile Asp Arg Leu Leu Gly Glu 210 215 220

Gly Phe Ser Asp Leu Phe Leu Thr Asp Gly Arg Ile Pro Ala Ala Met 225 230 235 240

Arg Leu Cys Thr Glu Glu Cys Arg Val Leu Gly His Ser Asp Gln Cys 245 250 255

Trp Met Pro Pro Leu Pro Ser Pro Ser Ser Asp Tyr Arg Ser Asn Met 260 265 270

Phe Ile Pro Gly Glu Glu Phe Pro Thr Gln Pro Gln Gln Gln His Pro
275 280 285

```
His Gln Ser Leu Glu Asp Asp Ala Gln Pro Ala Asp Ser Gly Glu Lys
                        295
Lys Lys Ser Phe Ser Thr Phe Gly Lys Asp Ser Pro Asn Asp Glu Asp
305
                    310
                                        315
Thr Gly Asp Thr Ser Thr Ser Ser Leu Leu Ser Glu Met Ser Ser Val
                325
Phe Gln Arg Leu Leu Pro Pro Ser Leu Asp Thr Tyr Ser Glu Cys Ser
Glu Val Asp Arg Ser Asn Ser Leu Glu Arg Arg Lys Gly Pro Leu Pro
                            360
Ala Lys Thr Val Gly Tyr Pro Gln Gly Val Ala Ala Trp Ala Ala Ser
Thr His Phe Gln Asn Pro Thr Thr Asn Cys Gly Pro Pro Leu Gly Thr
                                        395
His Ser Ser Val Gln Pro Ser Ser Lys Trp Leu Pro Ala Met Glu Glu
                405
                                    410
Ile Pro Glu Asn Tyr Glu Glu Asp Asp Phe Asp Asn Val Leu Asn His
                                425
Leu Asn Asp Gly Lys His Glu Leu Met Asp Ala Ser Glu Leu Val Ala
Glu Ile Asn Lys Leu Leu Gln Asp Val Arg Gln Ser
                        455
<210> 23
<211> 1219
<212> DNA
<213> Homo sapiens
<400> 23
gtggccattc ctcggtacag actagtcctg gtccttgggt gtgggcagtg ggggaggaac 60
caactggtcg aggtttcaga gccaaacctt gcctttggtt ggtgagtcct tgcccccag 120
geetgegete cacgatgeee tteaccettg geaateteag ggeeateetg ggtagtaace 180
ccactcetet etgetecege cegeacetgt ggeteteact etgggeteaa eccetgeaac 240
cctccaggag cccgacagca gccagctgcc tgcactgtcg cctccgtaag ctccaacttc 300
cagacccaga agtecetetg ettecetetg ttggaaaaag cetaaaagaa ttagetteca 360
gatteeteta geecetgete catteecace eagteettet gaagaggaat gageaataca 420
tctgagctgg atttctctct agtcctttct ccagacaaat ccttcttaaa gcaaaagtcc 480
tggctgagca cctgtccttg gggaccgatc tgccgtgtga ccaggggaag aaagttcccg 540
aaageetgtt ccaccaatte tgettetgtg ttgtgaatee agtetgettt ccattagaaa 600
accgcttcgg cacttatggt cactttaata aatctagtat gtaaaaaaag aaagaaagaa 660
aagaaacaga aaaacgtgca ggcaaatgta aaatacaatg ctctctgtaa gataaatatt 720
tgcctttttt tctaaaaggt gtacgtattc tgtatgtgaa attgtctgta gaaagtttct 780
atgttettaa atggeaatae atteeaaaaa ttgtaetgta gatatgtaea geaacegeae 840
tgggatgggg tagttttgcc tgtaatttta tttaaactcc agtttccaca cttgcatctt 900
gcaatgttgg tatggtatat atcagtgcaa aagaaaaaac aaaacaaaaa caaaaaaaa 960
aacaaaaaatc cacgcaggtc taaagcacag agtctgacgt acaaaaggaa aaatgctcag 1020
tattgaagtg tgtgaccttt gttgtaaatt acatctgtac tgtgaatgag aagtttttac 1080
aagtataata attgeettta ttacagetet ggetgagtgt teageetgag gatattett 1140
aaaaaaaaa gaattagcat gttggaataa atttgaaaat cccaaaaaaa aaaaaaaaa 1200
```

```
aaaaaaaaa aaaaaaaaa
                                                                   1219
<210> 24
<211> 78
<212> PRT
<213> Homo sapiens
<400> 24
Met Pro Phe Thr Leu Gly Asn Leu Arg Ala Ile Leu Gly Ser Asn Pro
                                     10
Thr Pro Leu Cys Ser Arg Pro His Leu Trp Leu Ser Leu Trp Ala Gln
                                  25
Pro Leu Gln Pro Ser Arg Ser Pro Thr Ala Ala Ser Cys Leu His Cys
                             40
Arg Leu Arg Lys Leu Gln Leu Pro Asp Pro Glu Val Pro Leu Leu Pro
                         55
                                          . 60
Ser Val Gly Lys Ser Leu Lys Glu Leu Ala Ser Arg Phe Leu
                     70
<210> 25
<211> 2411
<212> DNA
<213> Homo sapiens
<400> 25
ggccagaagg cggggagcca gaggcgccag gaccctagcg tggcgctcca gcaccccaga 60
ccgtggcggc gcctcgcctt agggaagagc aagggaagaa ctttatttga accgcgaaca 120
ttttttggtc actgagatcg agtctcccag tgctttggct tcccgcctct ttatcgtggg 180
tttgatccct gagctgctct cetttcccga acctcccggg gtgcagccta gagccctccc 240
gcgcggctga ctccagagta gaggaaggga ggcggcctcc ggctggtccc ccgaagccct 300
cgctgccccg cagatgcgga tggccagcca gtagcgggcg gtggccccgc gtcccgggag 360
cgcacagcaa tgcaggcgct taacattacc ccggagcagt tctctcggct gctgcgggac 420
cacaacctga cgcgggagca gttcatcgct ctgtaccggc tgcgaccgct cgtctacacc 480
ccagagetge egggaegege caagetggee etegtgetea eeggegtget eatettegee 540
ctggcgctct ttggcaatgc tctggtgttc tacgtggtga cccgcagcaa ggccatgcgc 600
acceptcacca acatetttat etgeteettg gegeteagtg acctgeteat cacettette 660
tgcattcccg tcaccatgct ccagaacatt tccgacaact ggctgggggg tgctttcatt 720
tgcaagatgg tgccatttgt ccagtctacc gctgttgtga cagaaatcct cactatgacc 780
tgcattgctg tggaaaggca ccagggactt gtgcatcctt ttaaaatgaa gtggcaatac 840
accaaccgaa gggctttcac aatgctaggt gtggtctggc tggtggcagt catcgtagga 900
tcacccatgt ggcacgtgca acaacttgag atcaaatatg acttcctata tgaaaaggaa 960
cacatctgct gcttagaaga gtggaccagc cctgtgcacc agaagatcta caccaccttc 1020
atcettgtca teetetteet eetgeetett atggtgatge ttattetgta cagtaaaatt 1080
ggttatgaac tttggataaa gaaaagagtt ggggatggtt cagtgcttcg aactattcat 1140
ggaaaagaaa tgtccaaaat agccaggaag aagaaacgag ctgtcattat gatggtgaca 1200
gtggtggctc tctttgctgt gtgctgggca ccattccatg ttgtccatat gatgattgaa 1260
tacagtaatt ttgaaaagga atatgatgat gtcacaatca agatgatttt tgctatcgtg 1320
caaattattg gattttccaa ctccatctgt aatcccattg tctatgcatt tatgaatgaa 1380
aacttcaaaa aaaatgtttt gtctgcagtt tgttattgca tagtaaataa aaccttctct 1440
ccagcacaaa ggcatggaaa ttcaggaatt acaatgatgc ggaagaaagc aaagttttcc 1500
ctcagagaga atccagtgga ggaaaccaaa ggagaagcat tcagtgatgg caacattgaa 1560
gtcaaattgt gtgaacagac agaggagaag aaaaagctca aacgacatct tgctctctt 1620
aggtotgaac tggotgagaa ttotoottta gacagtgggo attaattata acaatatott 1680
cataattaat gcccttcaga ttgtaaccca aagagaaaat tattttgagc aaaggtcaaa 1740
```

tactcttttt attcttaaga tgatgacaag aagaaaacaa atcatgtttc cattaaaaaa 1800

PCT/US99/19351 WO 00/11015

```
tgacacgagg ctagtccaag tgcagtgatg tttacaacca attgatcaca atcatttaac 1860
agatttctgt gttccttctc attcccactg cttcacttga ctagccttaa aaaagcaaca 1920
tggaaggcca ggcacggtgg ctcatgcctg taatcccagc actttgggag gcctagacgg 1980
gcggatcacg aggtcaggag atcaaaacca tcctggctaa cacggtgaaa ccccatctct 2040
gctaaaaata caaaaattag ccgggcgtgg tggcgggcac ctgtagtccc agctacttgg 2100
gagecteagg egggagaatg gtgtgaacce gggaggegga gettgeagtg ateegagate 2160
atgccactgc actccagect gggcgaaaga gcgagactcc ccgtctcaaa aaaaattttt 2220
ttgaaaaatt cgtaaaccat acttttaaga ttatttcagt ggatttttaa aaatcttgta 2280
cagaaatcag ggttcttagc tagcagtttt tctcccacgc agtcactgta atgtgactat 2340
gtattgctag attgaataag aaaataaaat aatatcttct tccttgaaaa aaaaaaaaa 2400
aaaaaaaaa a
<210> 26
<211> 431
<212> PRT
<213> Homo sapiens
<400> 26
Met Gln Ala Leu Asn Ile Thr Pro Glu Gln Phe Ser Arg Leu Leu Arg
Asp His Asn Leu Thr Arg Glu Gln Phe Ile Ala Leu Tyr Arg Leu Arg
                                 25
Pro Leu Val Tyr Thr Pro Glu Leu Pro Gly Arg Ala Lys Leu Ala Leu
Val Leu Thr Gly Val Leu Ile Phe Ala Leu Ala Leu Phe Gly Asn Ala
Leu Val Phe Tyr Val Val Thr Arg Ser Lys Ala Met Arg Thr Val Thr
                     70
Asn Ile Phe Ile Cys Ser Leu Ala Leu Ser Asp Leu Leu Ile Thr Phe
                 85
Phe Cys Ile Pro Val Thr Met Leu Gln Asn Ile Ser Asp Asn Trp Leu
Gly Gly Ala Phe Ile Cys Lys Met Val Pro Phe Val Gln Ser Thr Ala
        115
                            120
Val Val Thr Glu Ile Leu Thr Met Thr Cys Ile Ala Val Glu Arg His
                        135
Gln Gly Leu Val His Pro Phe Lys Met Lys Trp Gln Tyr Thr Asn Arg
                    150
Arg Ala Phe Thr Met Leu Gly Val Val Trp Leu Val Ala Val Ile Val
Gly Ser Pro Met Trp His Val Gln Gln Leu Glu Ile Lys Tyr Asp Phe
Leu Tyr Glu Lys Glu His Ile Cys Cys Leu Glu Glu Trp Thr Ser Pro
                                                205
Val His Gln Lys Ile Tyr Thr Thr Phe Ile Leu Val Ile Leu Phe Leu
   210
```

220

Leu Pro Leu Met Val Met Leu Ile Leu Tyr Ser Lys Ile Gly Tyr Glu 225 230 Leu Trp Ile Lys Lys Arg Val Gly Asp Gly Ser Val Leu Arg Thr Ile 250 His Gly Lys Glu Met Ser Lys Ile Ala Arg Lys Lys Lys Arg Ala Val 265 Ile Met Met Val Thr Val Val Ala Leu Phe Ala Val Cys Trp Ala Pro 280 Phe His Val Val His Met Met Ile Glu Tyr Ser Asn Phe Glu Lys Glu 295 Tyr Asp Asp Val Thr Ile Lys Met Ile Phe Ala Ile Val Gln Ile Ile 305 310 Gly Phe Ser Asn Ser Ile Cys Asn Pro Ile Val Tyr Ala Phe Met Asn 330 Glu Asn Phe Lys Lys Asn Val Leu Ser Ala Val Cys Tyr Cys Ile Val 340 345 Asn Lys Thr Phe Ser Pro Ala Gln Arg His Gly Asn Ser Gly Ile Thr 360 Met Met Arg Lys Lys Ala Lys Phe Ser Leu Arg Glu Asn Pro Val Glu Glu Thr Lys Gly Glu Ala Phe Ser Asp Gly Asn Ile Glu Val Lys Leu 390 395 Cys Glu Gln Thr Glu Glu Lys Lys Lys Leu Lys Arg His Leu Ala Leu 410 Phe Arg Ser Glu Leu Ala Glu Asn Ser Pro Leu Asp Ser Gly His 420 425 <210> 27 <211> 1945 <212> DNA <213> Homo sapiens <400> 27 atcatgccac tcatttcaga acttgagcaa aacagggcag tcaggatctg atgtctttct 60 ggtctcccta agaaaactaa gctcttgagg gacagccctt ggcaatgctt tcctatctgc 120 tgagcatggt gaccttcctt aggacttcca gagttcagtt ccttctggca gagaggtttt 180 ctttctccat gccatatgga tgtgactcaa atgaggggtc ccacagcttt tcctggctac 240 cacttgctgt gaccttatac atgttggggt ttgctcttaa agaggagagc aggaagaaag 300 gttggtttca gaaaccaaga gggtcggcag tggacgcgta cattttgtca cggagtccac 360 agagetgage tittgageag actetgagaa gtateattge tigigtigaa agaatacaae 420

aggatttaag tttctcttta aaaattgcac tgaagaaagg ccgggcgcg tggctcccc 480 tgtaatccaa gcgctttggg aggccgaggc gggggatca cgaggtcaag agatcgagac 540 catcctggcc aacatggtga aaccccgtct ctaataaaaa tacaaaaatt agccgggcat 600 ggtgacgtgc acctgtagtc ccagctacta gataggctga ggcaggagaa ttgcttgaat 660 ccgggaggcg gaggttgcag tgagccgaga tcgtgcact gaactccaac ctgccaatag 720 agcgagaactc cgtctcaaaa aaaaaaaaa aaaagaaaga aatagcattg aagaaaatac 780 cgcacatcag aggaaagctt atttctgca tggtgtcttt tcaaagatag aatatttgaa 840

```
gcatgttttc tagcgattgt gtgaatgagg gtgagctggc tgaggcatcg ctcaagctgq 900
ggggtggtgt gtaagaagca cgtggagcca caagaggcac ctcctatagt cagctaaggg 960
cttccctttc tgcgcccagc ttttgggtga agggtgattt ctactagaca catctgtgct 1020
teagteatag atgttaatag aggaageagt tttcctgctg cagattectg aatagagttg 1080
ctgaaagagt ctacttctgg actcgggaag ttgaaggcca gtctgtgtag aaaggctgag 1140
gcaacgggga aagacctgac agctagttac atacgctctg acatagtact cccatgatgg 1200
cttccagtga cacatgtgct gatagaattc taaacctctg gaatttccct gctggcgact 1260
tctatggccg ttgactgtac agggtaacct gatgccagat gctatgggcg tgatgagaac 1320
tagagcattg cagcatggag gaaactgtga ggcaccagat cctgtgcttc tgcaggccat 1380
tttctgaaaa cccctgttag gaaggttgga tttggcgtga cttgcttgag caagagtcct 1440
ggggagagat tttgaggttt aatttaacgg tatatccaga gctaacagtg actcaactcg 1500
tctagttctg caagtcagat gtatacttag agtctctctg tgaagggttt gggtctgagc 1560
tgtatagtat gtcaaactgc cagtaagcca gcccctcacc ctctgataga tattccttta 1620
atgcaccaga cttcatgttt gataaatgat taatggttga aattgtttct cttctttgt 1680
gttttcccag ttaatagatg gtcactgttt ccacaatgtt ttatactttc agctttttgt 1740
aacttaacta taattactta attttatttt tttaaagctt gttgtggtct aatgagaagt 1800
atttttcagt gcataatgtt tttctgagct tctgtaaatg ccatcccaat gtggtttggt 1860
aaaaaaaaa aaaaaaaaaa aaaaa
<210> 28
<211> 87
<212> PRT
<213> Homo sapiens
<400> 28
Met Leu Ser Tyr Leu Leu Ser Met Val Thr Phe Leu Arg Thr Ser Arg
Val Gln Phe Leu Leu Ala Glu Arg Phe Ser Phe Ser Met Pro Tyr Gly
                                25
Cys Asp Ser Asn Glu Gly Ser His Ser Phe Ser Trp Leu Pro Leu Ala
                            40
Val Thr Leu Tyr Met Leu Gly Phe Ala Leu Lys Glu Glu Ser Arg Lys
                        55
Lys Gly Trp Phe Gln Lys Pro Arg Gly Ser Ala Val Asp Ala Tyr Ile
Leu Ser Arg Ser Pro Gln Ser
                85
<210> 29
<211> 2184
<212> DNA
<213> Homo sapiens
<400> 29
gggcgccctc tggggctccg agcccggcgg gaccatgttc accagcaccg gctccagtgg 60
gctctacaag gcgcctctgt cgaagagcct tctgctggtc cccagtgccc tctccctcct 120
gctcgccctc ctcctgcctc actgccagaa gctctttgtg tatgaccttc acgcagtcaa 180
gaacgacttc cagatttgga ggttgatatg tggaagaata atttgccttg atttgaaaga 240
tactttttgc agtagtctgc ttatttataa ttttaggata tttgaaagaa gatatggaag 300
cagaaaattt gcatcctttt tgctgggttc ctgggttttg tcagccttat ttgactttct 360
cctcattgaa gctatgcagt atttctttgg catcactgca gctagtaatt tgccttctgg 420
attectggca cetgtgtttg etetgtttgt accattttae tgetecatae caagagteca 480
agtggcacaa attctgggtc cgttgtccat cacaaacaag acattgattt atatattggg 540
```

```
actgcagett ttcacetetg gttcctacat etggattgta gecataagtg gaettatgte 600
 eggtetgtge tacgacagea aaatgtteea ggtgcateag gtgetetgea tecceagetg 660
 gatggcaaaa ttctttctt ggacacttga acccatcttc tcttcttcag aacccaccag 720
 cgaagccaga attgggatgg gagccacgct ggacatccag agacagcaga gaatggagct 780
 gctggaccgg cagctgatgt teteteagtt tgcacaaggg aggcgacaga gacagcagca 840
 gggaggaatg atcaattgga atcgtctttt tcctccttta cgtcagcgac aaaacgtaaa 900
 ctatcagggc ggtcggcagt ctgagccagc agcgcccct ctagaagttt ctgaggaaca 960
 ggtcgcccgg ctcatggaga tgggattttc cagaggtgat gctttggaag ccctgagagc 1020
 ttcaaacaat gacctcaatg tcgccaccaa cttcctgctg cagcactgat agtcccaggc 1080
caacactggg accggaccgg cagccgagtg acagtgcgtg gtccccacca tcagatcagc 1140
ccggggaccg agcatctctg gtgctgatgt tcttgtggga agagggaggt tccaccgcac 1200
ccctgccctc aaccgcaaga ctgttgccgt tttagtgtgg agataagttt gccattacat 1260
tagcatgtat tttctatcta tatttttatt gggcattttc cctaggttgg agagtcagca 1320
ctcgttttga atgtgtttaa aatgcattaa aatggaagat ttctgcaggc agttgaatgg 1380
cactccagat ggggaattgc tgtaaccctc ttactgtaac atgtcatctc ctgcgtcgtg 1440
atggggagag ggtaatgtta cttcacaaag gacatgtcag atccttcttc atggactttt 1500
ttagttactg ttttttctct caaacttgtt ttcgaatctc ctgggagtga gggagaaaca 1560
gggagetgaa teeteeceea agetgtteea ggeeagagga etetgeagta getteteeta 1620
catctagtaa caaagaatgg tgataaccat gcactggttc aaggttctgg agttctccat 1680
gaaacttggg ttaattttgc tcagagtatc cagagttagc cactaggctg cgggtgaaat 1740
gggatggaga agaacaacag caggetteet ggagecacat gggetgacta gggeactetg 1800
tggctggcat ggcatgggct cagcccagga agaggagaaa cgatcccttg cctgccctc 1860
cetgtggcag ggetaactge etggeeetee tggetegcag ceagecagee ecetggcage 1920
aggtteteet cagggettgg gtetteaace tgtggegaca ggaggeaggg cagactgtgg 1980
aggacaggat gcaggtcagg gagagggaag gcaggggtgg accgccatga gcatgaaaag 2040
accegaagea agttgaetet tgeaatgtge aactgttatg ttetgeaaaa tgageaaega 2100
tgtatcaaat tgatgcaaat ttagatgttg atacttacaa taaagttttt aatgtgtttt 2160
aaaaaaaaaa aaaaaaaaaa aaaa
<210> 30
<211> 344
<212> PRT
<213> Homo sapiens
<400> 30
Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser
                                     10
Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu Ala Leu
                                 25
Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val
Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys
Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe
                     70
                                         75
Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu
                                     90
```

Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser

Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser

Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Glu

130 135 140 Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr 150 155 Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys 185 190 Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser 200 Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser 215 Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp 230 Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe 245 Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gln Gly Gly Met 270 Ile Asn Trp Asn Arg Leu Phe Pro Pro Leu Arg Gln Arg Gln Asn Val 280 Asn Tyr Gln Gly Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu 295 Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg 310 Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val 325 330 Ala Thr Asn Phe Leu Leu Gln His 340 <210> 31 <211> 2880 <212> DNA <213> Homo sapiens <400> 31 ccggcgtccg ggcgcgctgg agaggacgcg aggagccatg aggcgccagc ctgcgaaggt 60 ggcggcgctg ctgctcgggc tgctcttgga gtgcacagaa gccaaaaagc attgctggta 120 tttcgaagga ctctatccaa cctattatat atgccgctcc tacgaggact gctgtggctc 180 caggtgctgt gtgcgggccc tctccataca gaggctgtgg tacttctggt tccttctgat 240 gatgggcgtg cttttctgct gcggagccgg cttcttcatc cggaggcgca tgtaccccc 300 geegetgate gaggageeag cetteaatgt gteetacace aggeageece caaateeegg 360 cccaggagcc cagcagccgg ggccgcccta ttacaccgac ccaggaggac cggggatgaa 420 ccctgtcggg aattccatgg caatggcttt ccaggtccca cccaactcac cccaggggag 480 tgtggcctgc ccgccccctc cagcctactg caacacgcct ccgcccccgt acgaacaggt 540 agtgaaggcc aagtagtggg gtgcccacgt gcaagaggag agacaggaga gggcctttcc 600 ctggcctttc tgtcttcgtt gatgttcact tccaggaacg gtctcgtggg ctgctaaggg 660 cagtteetet gatateetea cageaageae agetetettt caggetttee atggagtaca 720

PCT/US99/19351 WO 00/11015

```
atatatgaac toacactttg totoctotgt tgcttctgtt tctgacgcag tctgtgctct 780
cacatggtag tgtggtgaca gtccccgagg gctgacgtcc ttacggtggc gtgaccagat 840
ctacaggaga gagactgaga ggaagaaggc agtgctggag gtgcaggtgg catgtagagg 900
ggccaggccg agcatcccag gcaagcatcc ttctgcccgg gtattaatag gaagcccat 960
gccgggcggc tcagccgatg aagcagcagc cgactgagct gagcccagca ggtcatctgc 1020
tccagcctgt cetetegtca gcetteetet tccagaaget gttggagaga cattcaggag 1080
agagcaagcc cettgtcatg tttctgtctc tgttcatatc ctaaagatag acttctcctg 1140
caccgccagg gaagggtagc acgtgcagct ctcaccgcag gatggggcct agaatcaggc 1200
ttgccttgga ggcctgacag tgatctgaca tccactaagc aaatttattt aaattcatgg 1260
gaaatcactt cctgccccaa actgagacat tgcattttgt gagctcttgg tctgatttgg 1320
agaaaggact gttacccatt tttttggtgt gtttatggaa gtgcatgtag agcgtcctgc 1380
cctttgaaat cagactgggt gtgtgtcttc cctggacatc actgcctctc cagggcattc 1440
tcaggcccgg gggtctcctt ccctcaggca gctccagtgg tgggttctga agggtgcttt 1500
caaaacgggg cacatctggc tgggaagtca catggactct tccagggaga gagaccagct 1560
gaggcgtctc tctctgaggt tgtgttgggt ctaagcgggt gtgtgctggg ctccaaggag 1620
gaggagettg etgggaaaag acaggagaag tactgactca actgcactga ccatgttgtc 1680
ataattagaa taaagaagaa gtggtcggaa atgcacattc ctggatagga atcacagctc 1740
accccaggat ctcacaggta gtctcctgag tagttgacgg ctagcgggga gctagttccg 1800
ccgcatagtt atagtgttga tgtgtgaacg ctgacctgtc ctgtgtgcta agagctatgc 1860
agettagetg aggegeetag attactagat gtgctgtate aeggggaatg aggtgggggt 1920
gettattttt taatgaacta atcagageet ettgagaaat tgttaeteat tgaactggag 1980
catcaagaca totoatggaa gtggatacgg agtgatttgg tgtccatgct tttcactctg 2040
aggacattta atcggagaac ctcctgggga attttgtggg agacacttgg gaacaaaaca 2100
gacaccctgg gaatgcagtt gcaagcacag atgctgccac cagtgtctct gaccaccctg 2160
gtgtgactgc tgactgccag cgtggtacct cccatgctgc aggcctccat ctaaatqaqa 2220
caacaaagca caatgttcac tgtttacaac caagacaact gcgtgggtcc aaacactcct 2280
cttcctccag gtcatttgtt ttgcattttt aatgtcttta ttttttgtaa tgaaaaagca 2340
cactaagctg cccctggaat cgggtgcagc tgaataggca cccaaaagtc cgtgactaaa 2400
tttcgtttgt ctttttgata gcaaattatg ttaagagaca gtgatggcta gggctcaaca 2460
attttgtatt cccatgtttg tgtgagacag agtttgtttt cccttgaact tggttagaat 2520
tgtgctactg tgaacgctga tcctgcatat ggaagtcccg cttcggtgac atttcctggc 2580
cattettgtt tecattgtgt ggatggtggg ttgtgeecae tteetggagt gagacagete 2640
ctggtgtgta gaattcccgg agcgtccgtg gttcagagta aacttgaagc agatctgtgc 2700
atgettttet etgeaacaat tggetegttt etettttttg ttetettttg ataggateet 2760
<210> 32
<211> 172
<212> PRT
<213> Homo sapiens
<400> 32
Met Arg Arg Gln Pro Ala Lys Val Ala Ala Leu Leu Leu Gly Leu Leu
                 5
Leu Glu Cys Thr Glu Ala Lys Lys His Cys Trp Tyr Phe Glu Gly Leu
Tyr Pro Thr Tyr Tyr Ile Cys Arg Ser Tyr Glu Asp Cys Cys Gly Ser
Arg Cys Cys Val Arg Ala Leu Ser Ile Gln Arg Leu Trp Tyr Phe Trp
Phe Leu Leu Met Met Gly Val Leu Phe Cys Cys Gly Ala Gly Phe Phe
                    70
Ile Arg Arg Arg Met Tyr Pro Pro Pro Leu Ile Glu Glu Pro Ala Phe
                85
```

90

```
Asn Val Ser Tyr Thr Arg Gln Pro Pro Asn Pro Gly Pro Gly Ala Gln
                                105
Gln Pro Gly Pro Pro Tyr Tyr Thr Asp Pro Gly Gly Pro Gly Met Asn
        115
Pro Val Gly Asn Ser Met Ala Met Ala Phe Gln Val Pro Pro Asn Ser
                        135
Pro Gln Gly Ser Val Ala Cys Pro Pro Pro Pro Ala Tyr Cys Asn Thr
                    150
Pro Pro Pro Pro Tyr Glu Gln Val Val Lys Ala Lys
                165
<210> 33
<211> 3406
<212> DNA
<213> Homo sapiens
<400> 33
taaagaacaa tootttaagg gagaacotag aagcoattoa acaaggttaa aatottoagg 60
cttccgagga tttggtagac agatcagagg cacgtttccc acaactgcga agaggcgctg 120
aggcaattet gcaagaagat tttggggttt tggaaaagaa gctatggaaa acggaggggc 180
aggeactetg cagataagge aagteetget tttetttgtt ttgetgggaa tgteteagge 240
gggctctgaa actgggaact ttttggtgat ggaggaattg cagagcggga gctttgtagg 300
aaatttggca aagaccctgg gactcgaggt gagtgagctg tcttcgcggg gggctcgggt 360
ggtttctaat gataacaaag agtgtttgca gctggacaca aacactgggg atttgctcct 420
gagagaaatg ctagacaggg aggagctctg tggctccaat gagccttgtg tgctgtattt 480
ccaagtgtta atgaaaaacc ccacgcagtt tttacaaatt gagctccagg tcagggatat 540
aaatgatcac tetecegtet tettggaaaa agaaatgete ttagaaatee cagagaacag 600
teetgttggt getgtgttet tgettgaaag tgeaaaggat ttagatgtag gaateaatge 660
tgtaaaaagc tacacaataa atccgaactc tcatttccac gttaaaataa gagtcaatcc 720
agacaatagg aaataccctg agttagttct ggacaaggcg ctggattatg aagagcgccc 780
ggageteagt tteateetea etgetetgga tggegggtee eeteeeaggt etggaactge 840
cttggtcagg gtggttggttg tagatattaa tgacaactcc cctgagtttg agcaggcttt 900
ttatgaggtg aagattctgg agaatagcat ccttggctcc ctggttgtga ccgtctcagc 960
ctgggattta gactctggaa caaacagtga actatcctat accttttccc atgcctcaga 1020
agatattcgc aagacatttg aaattaatca aaagtctggt gacattactt taacaqcacc 1080
tttggatttt gaagcaattg agtcatactc aataatcatt caagccacag atgggggagg 1140
actttttgga aaatctacag tcagaattca ggtgatggat gtaaacgaca acgctcctga 1200
aatcactgtg tcatcaatta ccagtccaat cccagaaaac actccagaga ctgtggttat 1260
ggttttcagg atacgagaca gagactctgg ggacaacgga aagatggttt gttctatccc 1320
ggaggacatc ccattcgtgc taaaatcttc ggtaaataat tactacactt tggaaacaga 1380
gagaccgctg gacagagaga gcagagccga gtacaacatc accatcaccg tcaccgactt 1440
ggggaccccc aggctaaaaa ccgagcacaa cataaccgtg ctggtctccg acgtcaatga 1500
caacgccccc gccttcaccc aaacttccta cgccctgttc gtccgcgaga acaacagccc 1560
cgccctgcac atcggcagca tcagcgccac agacagagac tcgggcacca acgcccaggt 1620
caactactcg ctgctgccgt cccaggaccc gcacctgccc ctcgcctccc tggtctccat 1680
caacgeggac aacggccacc tgtttgccct caggtcgctg gactacgagg ccctgcaggg 1740
gttccagttc cgcgtgggcg ccacagacca cggctccccg gctttgagca gcgaggcgct 1800
ggtgcgcgtg ctggtgctgg acgccaacga caactcgccc ttcgtgctgt acccgctgca 1860
gaacggctcc gcgccctgca ccgagctggt gccctgggcg gccgagccgg gctacctggt 1920
gaccaaggtg gtggcggtgg acggtgactc gggccagaac gcctggctgt cgtaccagct 1980
gctcaaggcc acggagcccg ggctattcgg cgtgtgggcg cacaatggcg aggtgcgcac 2040
cgccaggctg ctgagcgagc gcgacgcggc caagcacagg ctggtggtgc tggtcaagga 2100
caatggcgag ceteegeget eggecaeege caegetgeae gtgeteetgg tggaeggett 2160
eteccageee tacetgeete teeeggagge ggeeeeggee caggeecagg ecgaeteget 2220
```

```
cactgtctac ctggtggtgg cgttggcctc agtgtcgtcg ctcttcctct tctcggtgct 2280
cctgttcgtg gcggtgcggc tgtgcaggag gagcagggcg gccccggtcg gtcgctgctc 2340
ggtgcctgag ggcccctttc caggacatct ggtggacgtg agtggcaccg ggaccctgtc 2400
ccagagetac cactatgagg tgtgtgtgac tggaggetec aggtcaaata agttcaaatt 2460
tetgaaacca attateecca aetteetace ecagageaca ggtagtgaag tegaagaaaa 2520
tcccccattt cagaataatt tgggtttctg ataaagaatg aaaaataaaa cctgtgttta 2580
tgaatacatt tataattagg aacttatcgt gaggtgcctg taaagtagta tttttgatca 2640
cttcaaatac atactcttca agtcaagaaa taaatttctt tacatagaaa aggatacaga 2700
tttagtacca agaacacttc acaaagcagg aaatgtgcat gtgtaatggt ttatgtcaaa 2760
caattatgct taatataaag tctattaagt ggtaagtctt gtttgagata ttttaaattg 2820
ctttccattg ttttcaatat ttactgtgac ttttgttttc tgagttgatt agaatgctgt 2880
tcgagtatac ctaccctagt ttcagaagca tagattgtag tgtacctttt taaactttat 2940
ttttttaaaa aaagttgttt tatgaatcat acactatttt cacactttta atctcagaag 3000
aaacatatgt gacatggtat tttagtaatg accaaataga cggtcttaga gattcagtaa 3060
gttcactaag gtccactaac taataagtga caaaactgag catccatcct agatctgcct 3120
gactctaagt cagtgacttt gctcccattc catactgttt ttgtcattgg atatcacctg 3180
gcaagtttct gcctaactaa agagaagaaa agtttttatc gtattcatac tactgttcaa 3240
totttattta gaaataaact ttatctatga tttcattttc ttataaacca gtaatcttgc 3300
ttttctgggt aaattttcag ctattattac taatgctctg atctgcccaa atcttaagta 3360
aaaaaaaaa ttgaaagagc aaaaaaaaaa aaaaaaaa aaaaaa
<210> 34
<211> 795
<212> PRT
<213> Homo sapiens
Met Glu Asn Gly Gly Ala Gly Thr Leu Gln Ile Arg Gln Val Leu Leu
Phe Phe Val Leu Leu Gly Met Ser Gln Ala Gly Ser Glu Thr Gly Asn
             20
Phe Leu Val Met Glu Glu Leu Gln Ser Gly Ser Phe Val Gly Asn Leu
Ala Lys Thr Leu Gly Leu Glu Val Ser Glu Leu Ser Ser Arg Gly Ala
                        55
Arg Val Val Ser Asn Asp Asn Lys Glu Cys Leu Gln Leu Asp Thr Asn
Thr Gly Asp Leu Leu Arg Glu Met Leu Asp Arg Glu Glu Leu Cys
Gly Ser Asn Glu Pro Cys Val Leu Tyr Phe Gln Val Leu Met Lys Asn
            100
Pro Thr Gln Phe Leu Gln Ile Glu Leu Gln Val Arg Asp Ile Asn Asp
                            120
His Ser Pro Val Phe Leu Glu Lys Glu Met Leu Leu Glu Ile Pro Glu
                        135
Asn Ser Pro Val Gly Ala Val Phe Leu Leu Glu Ser Ala Lys Asp Leu
                    150
Asp Val Gly Ile Asn Ala Val Lys Ser Tyr Thr Ile Asn Pro Asn Ser
               165
                                    170
```

His Phe His Val Lys Ile Arg Val Asn Pro Asp Asn Arg Lys Tyr Pro 185 Glu Leu Val Leu Asp Lys Ala Leu Asp Tyr Glu Glu Arg Pro Glu Leu 200 Ser Phe Ile Leu Thr Ala Leu Asp Gly Gly Ser Pro Pro Arg Ser Gly 215 Thr Ala Leu Val Arg Val Val Val Asp Ile Asn Asp Asn Ser Pro 235 Glu Phe Glu Gln Ala Phe Tyr Glu Val Lys Ile Leu Glu Asn Ser Ile 250 Leu Gly Ser Leu Val Val Thr Val Ser Ala Trp Asp Leu Asp Ser Gly 265 Thr Asn Ser Glu Leu Ser Tyr Thr Phe Ser His Ala Ser Glu Asp Ile Arg Lys Thr Phe Glu Ile Asn Gln Lys Ser Gly Asp Ile Thr Leu Thr 295 Ala Pro Leu Asp Phe Glu Ala Ile Glu Ser Tyr Ser Ile Ile Gln 310 Ala Thr Asp Gly Gly Leu Phe Gly Lys Ser Thr Val Arg Ile Gln 330 Val Met Asp Val Asn Asp Asn Ala Pro Glu Ile Thr Val Ser Ser Ile 345 Thr Ser Pro Ile Pro Glu Asn Thr Pro Glu Thr Val Val Met Val Phe 360 Arg Ile Arg Asp Arg Asp Ser Gly Asp Asn Gly Lys Met Val Cys Ser 375 Ile Pro Glu Asp Ile Pro Phe Val Leu Lys Ser Ser Val Asn Asn Tyr 395 Tyr Thr Leu Glu Thr Glu Arg Pro Leu Asp Arg Glu Ser Arg Ala Glu 410 Tyr Asn Ile Thr Ile Thr Val Thr Asp Leu Gly Thr Pro Arg Leu Lys 425 Thr Glu His Asn Ile Thr Val Leu Val Ser Asp Val Asn Asp Asn Ala Pro Ala Phe Thr Gln Thr Ser Tyr Ala Leu Phe Val Arg Glu Asn Asn 455 Ser Pro Ala Leu His Ile Gly Ser Ile Ser Ala Thr Asp Arg Asp Ser 475 Gly Thr Asn Ala Gln Val Asn Tyr Ser Leu Leu Pro Ser Gln Asp Pro 485 490

ŀ	lis	Leu	Pro	Leu 500	Ala	Ser	Leu	Val	Ser 505	Ile	Asn	Ala	Asp	Asn 510	Gly	His
I	₋eu	Phe	Ala 515	Leu	Arg	Ser	Leu	Asp 520	Tyr	Glu	Ala	Leu	Gln 525	Gly	Phe	Gln
F	Phe	Arg 530	Val	Gly	Ala	Thr	Asp 535	His	Gly	Ser	Pro	Ala 540	Leu	Ser	Ser	Glu
	11a 545	Leu	Val	Arg	Val	Leu 550	Val	Leu	Asp	Ala	Asn 555	Asp	Asn	Ser	Pro	Phe 560
V	7al	Leu	Tyr	Pro	Leu 565	Gln	Asn	Gly	Ser	Ala 570	Pro	Cys	Thr	Glu	Leu 575	Val
				580		Pro			585					590		
			595			Gln		600					605			
		610				Leu	615					620				
6	25					Leu 630					635					640
					645	Asp				650					655	
				660		Leu			665					670		
			675		•	Pro		680					685			
		690				Leu	695					700				
7	05					Ala 710 Ser					715					720
					725	Thr				730					735	
				740		Gly			745					750		
			755			Phe		760					765			
		770					775					780	ser.	GIU	vaı	GIU
	85	ASII	FT.O	FEO	Fne	Gln 790	ASI	ASN	Leu	СТĀ	795					

<210> 35 <211> 3809

<212> DNA <213> Homo sapiens

<400> 35 ggggaccgga gtggggagcg cggcgtggag gtgccacccg gcgcgggtgg cggagagatc 60 agaagcetet teeccaagee gagecaacet eageggggae eegggeteag ggaegeggeg 120 geggeggegg egaetgeagt ggetggaega tggeagegte egeeggagee ggggeggtga 180 ttgcagcccc agacagccgg cgctggctgt ggtcggtgct ggcggcggcg cttgggctct 240 tgacagetgg agtateagee ttggaagtat atacgecaaa agaaatette gtggcaaatg 300 gtacacaagg gaagctgacc tgcaagttca agtctactag tacgactggc gggttgacct 360 cagtetectg gagettecag ccagaggggg ccgacactac tgtgtcgttt ttccactact 420 cccaagggca agtgtacctt gggaattatc caccatttaa agacagaatc agctgggctg 480 gagacettga caagaaagat gcatcaatca acatagaaaa tatgcagttt atacacaatg 540 gcacctatat ctgtgatgtc aaaaaccctc ctgacatcgt tgtccagcct ggacacatta 600 ggctctatgt cgtagaaaaa gagaatttgc ctgtgtttcc agtttgggta gtggtgggca 660 tagttactgc tgtggtccta ggtctcactc tgctcatcag catgattctg gctgtcctct 720 atagaaggaa aaactctaaa cgggattaca ctggggccca gtcatatatg cacagttaga 780 ccactccggc ggacatcaca gtgacaagat taacaagtca gagtctgtgg tgtatgcgga 840 tatccgaaag aattaagaga atacctagaa catatcctca gcaagaaaca aaaccaaact 900 ggactetegt geagaaaatg tageecatta ceacatgtag cettggagae ceaggeaagg 960 acaagtacac gtgtactcac agagggagag aaagatgtgt acaaaggata tgtataaata 1020 ttctatttag tcatcctgat atgaggagcc agtgttgcat gatgaaaaga tggtatgatt 1080 ctacatatgt acccattgtc ttgctgtttt tgtactttct tttcaggtca tttacaattg 1140 ggagatttca gaaacattcc tttcaccatc atttagaaat ggtttgcctt aatggagaca 1200 atagcagatc ctgtagtatt tccagtagac atggcctttt aatctaaggg cttaagactg 1260 attagtetta geatttactg tagttggagg atggagatge tatgatggaa geatacecag 1320 ggtggccttt agcacagtat cagtaccatt tatttgtctg ccgcttttaa aaaataccca 1380 ttggctatgc cacttgaaaa caatttgaga agtttttttg aagtttttct cactaaaata 1440 tggggcaatt gttagcctta catgttgtgt agacttactt taagtttgca cccttgaaat 1500 gtgtcatatc aatttctgga ttcataatag caagattagc aaaggataaa tgccgaaggt 1560 cactteatte tggacacagt tggatcaata etgattaagt agaaaateea agetttgett 1620 gagaactttt gtaacgtgga gagtaaaaag tatcggtttt attctttgct gatgtccttt 1680 ctgcttgaaa taacagtcac catacagcta aaggagagga gtttctttcc ttctaagtag 1740 gcagaaatgg tatcattatg ttgccgctct ccaatctccc agagctcgct ctctagagaa 1800 tcaccttctt tcgctttttt tttttttga ggtagagtct cactatgttg cccagactag 1860 cettgaacte ttgggetcaa gtgattetee etectcagee teeegagtag etggaacgaa 1920 ctatagttgc accactgcag ctggcaagaa tcaccttttt tataaagcgt cagtcatgct 1980 tccagcaaga ggcagcatca gtcatggctt tataacagct tcatggtgcc tcaaagactg 2040 ttgaggttaa tgagagccta gattagacag tttggctgtc cttccctaaa acttgttttc 2100 tcctattcac tactccccac cgcacttaaa atctatgagt ttttactttt tactgggaat 2160 ggaaagtgtg gtgaagatca ttcaacactt atgttgtcat ttctcccatt ttctgaattt 2220 ttttttaaat ttcccccctt ttaaaattgt tcgaaagccc acagttatgg aaagaattac 2280 tgtctagatg gtctgcagaa cgtgtttggg gtgagtggga gtgaggggca atgttacttt 2340 tteteettgt agtttggagt ccattatgag etgetgettt ttetteteat ettgteatet 2400 tctggggatg tttgaaggct gagttccaac agaattcaca aagggaataa aacaggattg 2460 agattttgag gtgtgcacaa ggtggtaaga taaagggcat atgagcttca aaactaatgc 2520 tgttgcatac atgaagcctt ttgttttttg aggagctatt tttgttattc ttgtaacgct 2580 ccaccttaca tgccacgtct gtgtgagtca acagggatca ggtttggtca ccacacatgt 2640 ctgaagctgg gcagcgtctg ctctgtgttc tgtgtggaat ggagaaaaaa acgcctgccc 2700 tgctgccttc catgttcata ggcccagccc aagagagtga cacacagtgc tggccctgag 2760 acatttccac aaagtggtca actctgcctt gcatcctaaa actttttggg catctatttt 2820 gaaaactata ggagcctttg gaaggcctct tatgtttgga ggggaagggt gttgagattg 2880 tcaccatcct tcaagctgag actcctggtg agcctttgcc accatgaaaa ccacatagct 2940 gaccagggct gtgcttgagg tacagaggac acacatcgta gacaggcctg tgtcatgttt 3000 ccttacagtc gttttttaca gagaaaaggg gcattgtttt ttcactgctt tctcaacagt 3060 tcctgtgaat aaatgaaaca tttcggagct ccctgagagc aagagccttc acttcttctt 3120 gcggtgccgg gaccatgtgt tggtgaagct ggtgctgtgg gggccactca ctcgaatgac 3180 acctggagge ctgttcctcc cttaccactc ccttccccag cccgacttct tggcctcctg 3240 cccaaccaga cacctcaaac tctgtcagcg ccctggcatt ctggcagaga atcctcacca 3300 gttctcacca accttccccc caggcaaggg cagctgccag catggtgctc tgccaggaca 3360

PCT/US99/19351 WO 00/11015

```
ggtttccctg aaggaagctg ctcacactga gatgagcctc tcagggcagg acctcttccc 3420
aagccctgca cacccacccc tgcagccctt ttggctcccc ttttccctgt gcctcagcac 3480
tcctttcctg gttgcagata acgaactaag gttgcctaaa gggcagatct gccctctcca 3540
tgtcttcgtc ctggcaaaca gggtcgtctt aaaattatgc gctaattctg tatgggagca 3600
ctcaaaaggc attacttaga gattgaaatt tcaaactatc tctagttttt caatggaaat 3660
atatcagcta gggaaaaacc atcaagctca ttattatttt ttgatcttca gttgtatttt 3720
aaaaaaaaa aaaaaaaaa
<210> 36
<211> 209
<212> PRT
<213> Homo sapiens
<400> 36
Met Ala Ala Ser Ala Gly Ala Gly Ala Val Ile Ala Ala Pro Asp Ser
Arg Arg Trp Leu Trp Ser Val Leu Ala Ala Ala Leu Gly Leu Leu Thr
Ala Gly Val Ser Ala Leu Glu Val Tyr Thr Pro Lys Glu Ile Phe Val
                           40
Ala Asn Gly Thr Gln Gly Lys Leu Thr Cys Lys Phe Lys Ser Thr Ser
Thr Thr Gly Gly Leu Thr Ser Val Ser Trp Ser Phe Gln Pro Glu Gly
Ala Asp Thr Thr Val Ser Phe Phe His Tyr Ser Gln Gly Gln Val Tyr
                85
Leu Gly Asn Tyr Pro Pro Phe Lys Asp Arg Ile Ser Trp Ala Gly Asp
Leu Asp Lys Lys Asp Ala Ser Ile Asn Ile Glu Asn Met Gln Phe Ile
His Asn Gly Thr Tyr Ile Cys Asp Val Lys Asn Pro Pro Asp Ile Val
Val Gln Pro Gly His Ile Arg Leu Tyr Val Val Glu Lys Glu Asn Leu
                   150
Pro Val Phe Pro Val Trp Val Val Val Gly Ile Val Thr Ala Val Val
Leu Gly Leu Thr Leu Leu Ile Ser Met Ile Leu Ala Val Leu Tyr Arg
                              185
Arg Lys Asn Ser Lys Arg Asp Tyr Thr Gly Ala Gln Ser Tyr Met His
                         200
Ser
```

<210> 37 <211> 1954

```
<212> DNA
 <213> Homo sapiens
 <400> 37
 gagacttggg ctggagccgc cctgggtgtc agcgggctcg gctcccgcgc acgctccggc 60
 cgtcgcgcag cctcggcacc tgcaggtccg tgcgtcccgc ggctggcgcc cctgactccg 120
 teceggecag ggagggecat gattteeete eeggggeeee tggtgaceaa ettgetgegg 180
 tttttgttcc tggggctgag tgccctcgcg ccccctcgc gggcccagct gcaactgcac 240
 ttgcccgcca accggttgca ggcggtggag ggaggggaag tggtgcttcc agcgtggtac 300
 accttgcacg gggaggtgtc ttcatcccag ccatgggagg tgccctttgt gatgtggttc 360
 ttcaaacaga aagaaaagga ggatcaggtg ttgtcctaca tcaatggggt cacaacaagc 420
 aaacctggag tatccttggt ctactccatg ccctcccgga acctgtccct gcggctggag 480
 ggtctccagg agaaagactc tggcccctac agctgctccg tgaatgtgca agacaaacaa 540
 ggcaaatcta ggggccacag catcaaaacc ttagaactca atgtactggt tcctccagct 600
 cctccatcct gccgtctcca gggtgtgccc catgtggggg caaacgtgac cctgagctgc 660
 cagtetecaa ggagtaagee egetgtecaa taccagtggg ateggeaget tecateette 720
 cagactttct ttgcaccage attagatgtc atccgtgggt ctttaagcct caccaacctt 780
 togtottoca tggotggagt ctatgtotgo aaggoodaca atgaggtggg cactgoodaa 840
 tgtaatgtga cgctggaagt gagcacaggg cctggagctg cagtggttgc tggagctgtt 900
ggcaaggccc tggaggagcc agccaatgat atcaaggagg atgccattgc tccccggacc 1020
ctgccctggc ccaagagctc agacacaatc tccaagaatg ggaccctttc ctctgtcacc 1080
teegeacgag ceeteeggee acceeatgge ecteecagge etggtgeatt gacceecacg 1140
cccagtctct ccagccaggc cctgccctca ccaagactgc ccacgacaga tggggcccac 1200
cctcaaccaa tatcccccat ccctggtggg gtttcttcct ctggcttgag ccgcatgggt 1260
getgtgeetg tgatggtgee tgeecagagt caagetgget etetggtatg atgaceceae 1320
cactcattgg ctaaaggatt tggggtctct ccttcctata agggtcacct ctagcacaga 1380
ggcctgagtc atgggaaaga gtcacactcc tgacccttag tactctgccc ccacctctct 1440
ttactgtggg aaaaccatct cagtaagacc taagtgtcca ggagacagaa ggagaagagg 1500
aagtggatet ggaattggga ggageeteea eecaeeeetg aeteeteett atgaageeag 1560
ctgctgaaat tagctactca ccaagagtga ggggcagaga cttccagtca ctgagtctcc 1620
caggececct tgatetgtac eccaececta tetaacacca ecettggete ecaetecage 1680
tecetgtatt gatataacet gteaggetgg ettggttagg ttttaetggg geagaggata 1740
gggaatetet tattaaaaet aacatgaaat atgtgttgtt tteatttgea aatttaaata 1800
aaaaaaaaaa aaaaaaaaaa aaaa
<210> 38
<211> 390
<212> PRT
<213> Homo sapiens
<400> 38
Met Ile Ser Leu Pro Gly Pro Leu Val Thr Asn Leu Leu Arg Phe Leu
                                  10
Phe Leu Gly Leu Ser Ala Leu Ala Pro Pro Ser Arg Ala Gln Leu Gln
            20
                              25
Leu His Leu Pro Ala Asn Arg Leu Gln Ala Val Glu Gly Glu Val
                          40
Val Leu Pro Ala Trp Tyr Thr Leu His Gly Glu Val Ser Ser Ser Gln
Pro Trp Glu Val Pro Phe Val Met Trp Phe Phe Lys Gln Lys Glu Lys
                   70
                                      75
Glu Asp Gln Val Leu Ser Tyr Ile Asn Gly Val Thr Thr Ser Lys Pro
```

85 90 Gly Val Ser Leu Val Tyr Ser Met Pro Ser Arg Asn Leu Ser Leu Arg 105 Leu Glu Gly Leu Gln Glu Lys Asp Ser Gly Pro Tyr Ser Cys Ser Val 120 Asn Val Gln Asp Lys Gln Gly Lys Ser Arg Gly His Ser Ile Lys Thr 135 Leu Glu Leu Asn Val Leu Val Pro Pro Ala Pro Pro Ser Cys Arg Leu Gln Gly Val Pro His Val Gly Ala Asn Val Thr Leu Ser Cys Gln Ser 170 Pro Arg Ser Lys Pro Ala Val Gln Tyr Gln Trp Asp Arg Gln Leu Pro Ser Phe Gln Thr Phe Phe Ala Pro Ala Leu Asp Val Ile Arg Gly Ser 200 Leu Ser Leu Thr Asn Leu Ser Ser Ser Met Ala Gly Val Tyr Val Cys 215 Lys Ala His Asn Glu Val Gly Thr Ala Gln Cys Asn Val Thr Leu Glu 235 Val Ser Thr Gly Pro Gly Ala Ala Val Val Ala Gly Ala Val Val Gly Thr Leu Val Gly Leu Gly Leu Leu Ala Gly Leu Val Leu Leu Tyr His 265 Arg Arg Gly Lys Ala Leu Glu Glu Pro Ala Asn Asp Ile Lys Glu Asp 280 Ala Ile Ala Pro Arg Thr Leu Pro Trp Pro Lys Ser Ser Asp Thr Ile 295 Ser Lys Asn Gly Thr Leu Ser Ser Val Thr Ser Ala Arg Ala Leu Arg 315 Pro Pro His Gly Pro Pro Arg Pro Gly Ala Leu Thr Pro Thr Pro Ser 330 Leu Ser Ser Gln Ala Leu Pro Ser Pro Arg Leu Pro Thr Thr Asp Gly 345 Ala His Pro Gln Pro Ile Ser Pro Ile Pro Gly Gly Val Ser Ser Ser 360 Gly Leu Ser Arg Met Gly Ala Val Pro Val Met Val Pro Ala Gln Ser 375 Gln Ala Gly Ser Leu Val

```
<210> 39
<211> 1933
<212> DNA
<213> Homo sapiens
<400> 39
ggggtggggc caggaggaag atggcggcgt ccgcagctgc cgctgagctc caggcttctg 60
ggggtccgcg gcacccagtg tgtctgttgg tgttgggaat ggcgggatcc gggaaaacca 120
cttttgtaca gaggeteaca ggacacetge atgeecaagg caetecaceg tatgtgatea 180
acctggatcc agcagtacat gaagttccct ttcctgccaa tattgatatt cgtgatactg 240
taaagtataa agaagtaatg aaacaatatg gacttggacc caatggcggc atagtgacct 300
cactcaatct ctttgctacc agatttgatc aggtgatgaa atttattgag aaggcccaga 360
acatgtccaa atatgtgttg attgacacac ctggacagat tgaggtattc acctggtcag 420
cttctgggac aattatcact gaagcccttg catcctcatt tccaacagtt gtcatctatg 480
taatggacac atcgagaagt accaacccag tgaccttcat gtccaacatg ctctatgcct 540
gcagcatctt atacaaaacc aagctgcctt tcattgtggt catgaataaa actgacatca 600
ttgaccacag ctttgcagtg gaatggatgc aggattttga ggctttccaa gatgccttga 660
atcaagagac tacatacgtc agtaacctga ctcgttcaat gagcctggtg ttagatgagt 720
tttacagete acteagggtg gtgggtgtet etgetgttet gggtaetgga ttagatgaac 780
tetttgtgca agttaccagt getgeegaag aatatgaaag ggagtategt eetgaatatg 840
aacgtctgaa aaaatcactg gccaacgcag agagccaaca gcagagagaa caactggaac 900
gccttcgaaa agatatgggt tctgtagcct tggatgcagg gactgccaaa gacagcttat 960
ctcctgtgct gcacccttct gatttgatcc tgactcgagg aaccttggat gaagaggatg 1020
aggaagcaga cagcgatact gatgacattg accacagagt tacagaggaa agccatgaag 1080
agccagcatt ccagaatttt atgcaagaat cgatggcaca atactggaag agaaacaata 1140
aataggagac tttagcacac ttcacttgtt tctagaagtc cagaattttg gacctccacg 1200
tgaaagaact gttcttacct ctgaactggg ggctcccata agggataatt ttcctcagag 1260
tagcaaagtt totottatta gagaaatott gtgactcaga tgaagtcagg gatagaagac 1320
ccttggacct ggcaggttaa tgctgattat tccttggcct ttcccttgta tttatgcaag 1380
gaaggatata ctgagctgat actcttccaa gcctacaact tcaagtttta tcatttgaac 1440
tcaagtactt ttgctgctga ggaatggaat caaaagaacg tagtctcctg gtaaccacct 1500
cagateteta ttattagget agatgtatag ectetaetee eccagettet tgetettgae 1560
cctgcactgt aagttgccct tctattagca gccaaggaaa agggaaacat gagcttatcc 1620
agaacggtgg cagagtetee ttggcaatea accaacgttg ctatgaaata tgeeteacae 1680
tgtatagctc attataggac gtcaggtttg ttgaaaaaag tgggcaagac atgattaatg 1740
aatcagaatc ctgtttcatt ggtgacttgg ataaagactt tttaatttta actttgaaaa 1800
aaaaaaaaa aaa
<210> 40
<211> 374
<212> PRT
<213> Homo sapiens
<400> 40
Met Ala Ala Ser Ala Ala Ala Glu Leu Gln Ala Ser Gly Gly Pro
Arg His Pro Val Cys Leu Leu Val Leu Gly Met Ala Gly Ser Gly Lys
            20
                               25
Thr Thr Phe Val Gln Arg Leu Thr Gly His Leu His Ala Gln Gly Thr
Pro Pro Tyr Val Ile Asn Leu Asp Pro Ala Val His Glu Val Pro Phe
                       55
Pro Ala Asn Ile Asp Ile Arg Asp Thr Val Lys Tyr Lys Glu Val Met
                   70
                                      75
```

Lys Gln Tyr Gly Leu Gly Pro Asn Gly Gly Ile Val Thr Ser Leu Asn 85 90 95

Leu Phe Ala Thr Arg Phe Asp Gln Val Met Lys Phe Ile Glu Lys Ala
100 105 110

Gln Asn Met Ser Lys Tyr Val Leu Ile Asp Thr Pro Gly Gln Ile Glu 115 120 125

Val Phe Thr Trp Ser Ala Ser Gly Thr Ile Ile Thr Glu Ala Leu Ala 130 135 140

Ser Ser Phe Pro Thr Val Val Ile Tyr Val Met Asp Thr Ser Arg Ser 145 150 155 160

Thr Asn Pro Val Thr Phe Met Ser Asn Met Leu Tyr Ala Cys Ser Ile
165 170 175

Leu Tyr Lys Thr Lys Leu Pro Phe Ile Val Val Met Asn Lys Thr Asp 180 185 190

Ile Ile Asp His Ser Phe Ala Val Glu Trp Met Gln Asp Phe Glu Ala 195 200 205

Phe Gln Asp Ala Leu Asn Gln Glu Thr Thr Tyr Val Ser Asn Leu Thr 210 220

Arg Ser Met Ser Leu Val Leu Asp Glu Phe Tyr Ser Ser Leu Arg Val 225 230 235 240

Val Gly Val Ser Ala Val Leu Gly Thr Gly Leu Asp Glu Leu Phe Val 245 250 255

Gln Val Thr Ser Ala Ala Glu Glu Tyr Glu Arg Glu Tyr Arg Pro Glu 260 265 270

Tyr Glu Arg Leu Lys Lys Ser Leu Ala Asn Ala Glu Ser Gln Gln Gln 275 280 285

Arg Glu Gln Leu Glu Arg Leu Arg Lys Asp Met Gly Ser Val Ala Leu 290 295 300

Asp Ala Gly Thr Ala Lys Asp Ser Leu Ser Pro Val Leu His Pro Ser 305 310 315 320

Asp Leu Ile Leu Thr Arg Gly Thr Leu Asp Glu Glu Asp Glu Glu Ala 325 330 335

Asp Ser Asp Thr Asp Asp Ile Asp His Arg Val Thr Glu Glu Ser His 340 345 350

Glu Glu Pro Ala Phe Gln Asn Phe Met Gln Glu Ser Met Ala Gln Tyr 355 360 365

Trp Lys Arg Asn Asn Lys

<210> 41

```
<211> 2795
 <212> DNA
 <213> Homo sapiens
 <400> 41
aaaaagctcg gcatggctga cgacgcgggt ttggagaccc cgctgtgttc cgagcagttc 60
ggctccgggg aggcacgggg ctgccgcgcc gccgcggacg ggagcctgca gtgggaggtc 120
gggggctggc gctggtgggg gctctccagg gccttcacgg tcaaacctga aggacgagat 180
gegggegaag tgggggette eggggeeeee teacegeee teteeggget eeaggeegtg 240
tteetgeete agggetteee tgatagegte ageceggaet acttgeeeta ceagetgtgg 300
gatteegtge aggegtttge tteeageete teeggeteee tageeaceea ggeagtettg 360
ctgggcatag gggtggggaa cgcaaaagcc actgtttcag ctgccacggc cacctggctc 420
gtgaaagatt caactggcat gctgggccgc atcgtctttg cctggtggaa agggagcaaa 480
ctggactgca atgccaagca gtggaggctt tttgcggaca tcctcaatga cgtagccatg 540
ttccttgaga ttatggctcc tgtataccca atctgtttca ccatgaccgt ctccaccage 600
aacctagcca agtgcatcgt gagtgttgct ggtggggcca ctcgggctgc cctgaccgtg 660
caccaggete ggaggaacaa catggetgae gtgteageea aggaeageag ceaggagaeg 720
ctggtgaacc tggcggggct cttggtcagc ctcctgatgc tccctctggt gtcaggttgc 780
cctggcttca gccttggatg tttcttcttc ctcactgccc tccacatcta cgccaactac 840
egegeggtee gageeetggt catggagace ttgaacgaag geeggeteeg getggteetg 900
aagcactacc ttcagagggg agaggtactc gacccaactg cagccaatcg catggagccg 960
ctgtggacag gtttctggcc agctccgtct ctatccctgg gggtcccctt acaccgcttg 1020
gtctccagtg tctttgagct gcagcagctg gttgaggggc accaagaatc ctacctcctc 1080
tgctgggacc agtcacaaaa ccaggtacag gtagttctga accagaaggc aggccccaag 1140
accatectaa gggccgccac acatgggctg atgettgggg ccctgcaggg agatggaccc 1200
cttccagcag agctggagga gctgaggaac cgggtgcggg caggtcctaa gaaagagagc 1260
tgggtcgtcg tcaaggagac acacgaagtg ttggacatgc tgttcccaaa gttcttgaaa 1320
ggactgcagg atgccggctg gaagaccgag aagcaccagc tagaggtgga tgagtggagg 1380
gccacatggc ttctgtctcc cgaaaagaag gtcttgtgag cagcccagac ggaggcccaa 1440
gcccagggca ggaacctgga gcaaggacac tttggccaca gcaggacagg ggaaaggcag 1500
ctttattttt ccttagggca actgcagcgg gtgggccagg ccctcatggg aagtgactgc 1560
caatcagatg cagtgggccc caggcagagg aaggccggga gaaggggagc caggaccttc 1620
teacceact geocettece ettttetggg gageacegea ggeteeteac ecceaettee 1680
tgtgaggctg tggcttatgg tgtccaacgc agttggtctt aggcatagaa gccccagagg 1740
aacacggcca ctgccatcat gagcagggca ttgaggttga ccacacgggc ccagctcggg 1800
tectegetga tgteeteeag eegeetgget getgeegetg eeteeteetg ggtaagggge 1860
ggaggactgc ccaccccacc tctgctcatt ccacaaaacc agagcaggca ctggcggaag 1920
aggettggtg ceggggeetg gggetetgag ggaaattgag geeetgeagt tagtttgegg 1980
gaactcagct ectecagece caceteccag catggtgeec taccattcat etccatggca 2040
ctctctgggc acccattctg tacagggagt gaggagcctt gctgctcatc agcatccagg 2100
tcctcccgtt cctccttgct atgccggaga ctgaagacca ggcggtggag ctggggaggg 2160
tgggagcacg aacgaggtgg gagttctgtc cccccatgcc tggccctaaa gtctcttgca 2220
caccageteg teactgeetg cectacecae etetgtecag tetacacae cageccagge 2280
ttaactcatg ccaactccac cctacatggc tgccctgtgc cctcgggata aaccccaagc 2340
ccctgagctt gtgtttaaag ccgttggcct tgctcccca gctttgtcag ctcaggtctg 2400
tctacaccca gatggtagcg cttgtgacac tggcctggca gtcctgctca cagtgttctg 2460
tgcctgtgtg ctcccaccct ttcctcctgc tgctgcagaa acccggccat ccttccacac 2520
ecagatetet tgteetgtee teaceceace etgeeaceat cagecetgee tggagecace 2580
tgccctttgg caacaaaacc aaaccttttt gtgggcgttc aagatggtat tgtgcccacc 2640
agtcagatcc tgtgttttga gtcccaaagg ccatgccaag gattggcttt gggaggcttt 2700
aatcaccaac ccatcaacat caagcctccc ccaggccggt tcaaataaat gtatttaaat 2760
aaaaaaaaaa aaaaaaaaa aaaaa
<210> 42
<211> 468
<212> PRT
<213> Homo sapiens
<400> 42
Met Ala Asp Asp Ala Gly Leu Glu Thr Pro Leu Cys Ser Glu Gln Phe
```

1				5					10					15	•
Gly	Ser	Gly	Glu 20	Ala	Arg	Gly	Cys	Arg 25		Ala	Ala	Asp	Gly 30		Leu
Gln	Trp	Glu 35	Val	Gly	Gly	Trp	Arg 40		Trp	Gly	Leu	Ser 45		Ala	Phe
Thr	Val 50	Lys	Pro	Glu	Gly	Arg 55	Asp	Ala	Gly	Glu	Val 60		Ala	Ser	Gly
Ala 65	Pro	Ser	Pro	Pro	Leu 70	Ser	Gly	Leu	Gln	Ala 75	Val	Phe	Leu	Pro	Gln 80
Gly	Phe	Pro	Asp	Ser 85	Val	Ser	Pro	Asp	Tyr 90	Leu	Pro	Tyr	Gln	Leu 95	
Asp	Ser	Val	Gln 100	Ala	Phe	Ala	Ser	Ser 105	Leu	Ser	Gly	Ser	Leu 110	Ala	Thr
Gln	Ala	Val 115	Leu	Leu	Gly	Ile	Gly 120	Val	Gly	Asn	Ala	Lys 125	Ala	Thr	Val
	130				Thr	135					140				
145					Ala 150					155					160
				165	Leu				170					175	
			180		Ala			185					190		
		195			Leu		200					205			
	210				Leu	215					220				
225					Lys 230					235					240
				245	Ser				250					255	
			260		Gly			265					270		
		275			Ala		280					285			
	290					295					300				
305					Ala 310					315					320
ne	rrp	Pro	Ala	Pro	Ser	Leu	Ser	Leu	Gly	Val	Pro	Leu	His	Arg	Leu

```
325
                                    330
                                                         335
Val Ser Ser Val Phe Glu Leu Gln Gln Leu Val Glu Gly His Gln Glu
                                345
Ser Tyr Leu Leu Cys Trp Asp Gln Ser Gln Asn Gln Val Gln Val Val
                            360
Leu Asn Gln Lys Ala Gly Pro Lys Thr Ile Leu Arg Ala Ala Thr His
                        375
                                            380
Gly Leu Met Leu Gly Ala Leu Gln Gly Asp Gly Pro Leu Pro Ala Glu
                                        395
Leu Glu Glu Leu Arg Asn Arg Val Arg Ala Gly Pro Lys Lys Glu Ser
                                    410
Trp Val Val Lys Glu Thr His Glu Val Leu Asp Met Leu Phe Pro
                                425
Lys Phe Leu Lys Gly Leu Gln Asp Ala Gly Trp Lys Thr Glu Lys His
                            440
Gln Leu Glu Val Asp Glu Trp Arg Ala Thr Trp Leu Leu Ser Pro Glu
    450
                        455
Lys Lys Val Leu
465
<210> 43
<211> 2980
<212> DNA
<213> Homo sapiens
<400> 43
aagaaaaact tttttgttat tgggctttcc aggtggagtt cagaaccagt gactcacact 60
tetcagteet gggagcaatt tatttgetae ttggaggggt tgtaagaaaa gccagtgaga 120
aagcagactc cccccacaac acagatccac tgtggacccc caaaacctgt cctgtccccc 180
tettttaaga eteeageeae eeetettggg etetetaett eeaeggggea eatgetgatg 240
eccetgtgtg ggetgetetg gtggtggtgg tgetgetget eeggetggta etgetatgga 300
ttgtgtgccc cagcccccca gatgttgcgc caccagggtc tcctcaagtg ccgctgccgc 360
atgetettea atgaeetgaa ggttttetta etgeggegee eteeteaage geeeetgeee 420
atgcacggcg acceccagee ecceggtttg geggecaaca acaccettee ggetetggge 480
gccggggggt gggcaggctg gaggggcccc cgagaagtgg tgggcaggga gccccctcct 540
gtgccacctc caccccctt gccaccttct tctgtggaag atgactgggg tggcccagcc 600
acagageeae etgeeteget geteageagt geeteeteag atgaettetg taaggagaag 660
accgaggate getactcact gggeageage ttggacagtg gtatgaggae eccaetetge 720
cgcatctgct tccaggggcc agaacagggg gagctgctga gcccatgccg ctgtgatggc 780
tcggtcaagt gcacacacca gccttgcctc atcaagtgga tcagcgagcg gggctgctgg 840
agetgegage tgtgetacta caagtaccae gteategeea taageacaaa aaateetetg 900
cagtggcagg ccatctctct gacggtcatt gagaaggttc aggttgcagc cgccatcctg 960
ggeteeetet teeteatege cagtatttet tggeteatet ggteaaettt cageeeteg 1020
gcaagatggc agcgccaaga cettetette cagatetget acgggatgta tggetteatg 1080
gacgtggtgt gcataggtct catcatccat gaaggaccct cggtgtaccg catctttaaa 1140
cggtggcagg ctgtcaacca gcagtggaaa gtgctgaact atgacaagac aaaagacctg 1200
gaggatcaaa aggcaggagg caggaccaac ccccggacct cctcatccac ccaggccaat 1260
atcccctcct cggaagagga gaccgcaggc acccctgccc ctgagcaggg ccctgcccag 1320
gctgccggcc acccctcagg ccctctgtcc catcaccact gtgcttatac catcctgcac 1380
atcctgagtc acttgagacc tcatgaacag cgaagtcccc caggcagcag ccgagagctg 1440
```

```
gtcatgagag tcacgacagt gtgagagcag aggcccggaa ggaaggccat gaccaccact 1500
gagggcccag agcagggtgg ggaggtgcag tggcaccccc ggagccaaca gagggagcag 1560
gcagagggtg ggggacctgg cgggagccct ggggtagtgt cagagcggga gtgaggctgg 1620
tgcaggagca gttctgctat ttccaatcag tcaatgccac tctccacaac aacaatgaaa 1680
accaacacca actcaacaac aaagtgcaat acaggctgaa cctggcccaa cagaaaaacc 1740
ctgccccaat gcacctgcag gcaaggtacc cgaagaagca gaggctgagg gcaggcaaag 1800
cctgtgtgac tgtggcagtg ccggaggcca agggggccaa gaggaaaagc atctgtggtc 1860
tgccctgctc tcaccctgtt tggttttgtt tctcctgggg ctgtgttctg caggcagcca 1920
gaaaaggagg aggcacgggt gagctggcag ggacacactg cctttggggc tcctgggctc 1980
atttggatgg gcaagattcg ctgacaaatg gctgtgggga tggtggggtg gatggtcagg 2040
gagggatgct cagggaggga tatgctggtg tgagcagcca gagggagagt gtgtctcctt 2100
cctgaaggaa cttccaaatg gaactcccga tttcaggtgg gctaaaagag ggcttaggtt 2160
tggaaaaggg tgtccttctg tgcccttgtt aatttatttt atagtgattt ggttcaaaga 2220
aagtacagat ttccagtgga tatttcaagc acagttctgc tgctgtggct tcagctttgg 2340
aagctgtcaa tcccggagca actttcccaa ctacccaacc ccaccatggc caggacatgt 2400
gcaatgccag ccccttcttg tcttggcaca tgcacagacc cagtcccctc acggtagggc 2460
accectgace tacgggette caagagagea getgeagtgg ttgggaggag ettgaceagt 2520
gtgccccaag gagtggagta gagcccaatc taagtattcc ttgctgcttg gaaccctccc 2580
tgtttggaac cetececaaa gaggeagtea ggetgatget cagtgetttg tgetecetge 2640
teetteeege gtagecaggt gggeccaagg gtgeetggea gggageacta eeeetggaee 2700
cetectgete getetgggga ecetgecagg gaaggecact gggtgtteae etgeaaagtt 2760
totggttgtc actgcacagt ggtcgcgtca tccatgggta ttaaaaggac actgtcaagt 2820
actttttaa actagttttt agggtttttt aaaactctct gttgtttgta atattctctt 2880
<210> 44
<211> 410
<212> PRT
<213> Homo sapiens
Met Leu Met Pro Leu Cys Gly Leu Leu Trp Trp Trp Trp Cys Cys Cys
Ser Gly Trp Tyr Cys Tyr Gly Leu Cys Ala Pro Ala Pro Gln Met Leu
                              25
Arg His Gln Gly Leu Leu Lys Cys Arg Cys Arg Met Leu Phe Asn Asp
Leu Lys Val Phe Leu Leu Arg Arg Pro Pro Gln Ala Pro Leu Pro Met
His Gly Asp Pro Gln Pro Pro Gly Leu Ala Ala Asn Asn Thr Leu Pro
                   70
Ala Leu Gly Ala Gly Gly Trp Ala Gly Trp Arg Gly Pro Arg Glu Val
Val Gly Arg Glu Pro Pro Pro Val Pro Pro Pro Pro Pro Leu Pro Pro
Ser Ser Val Glu Asp Asp Trp Gly Gly Pro Ala Thr Glu Pro Pro Ala
       115
                          120
Ser Leu Leu Ser Ser Ala Ser Ser Asp Asp Phe Cys Lys Glu Lys Thr
   130
                      135
```

Glu Asp Arg Tyr Ser Leu Gly Ser Ser Leu Asp Ser Gly Met Arg Thr

150 155 Pro Leu Cys Arg Ile Cys Phe Gln Gly Pro Glu Gln Gly Glu Leu Leu 170 Ser Pro Cys Arg Cys Asp Gly Ser Val Lys Cys Thr His Gln Pro Cys 180 185 Leu Ile Lys Trp Ile Ser Glu Arg Gly Cys Trp Ser Cys Glu Leu Cys 200 Tyr Tyr Lys Tyr His Val Ile Ala Ile Ser Thr Lys Asn Pro Leu Gln 215 Trp Gln Ala Ile Ser Leu Thr Val Ile Glu Lys Val Gln Val Ala Ala Ala Ile Leu Gly Ser Leu Phe Leu Ile Ala Ser Ile Ser Trp Leu Ile Trp Ser Thr Phe Ser Pro Ser Ala Arg Trp Gln Arg Gln Asp Leu Leu . 265 Phe Gln Ile Cys Tyr Gly Met Tyr Gly Phe Met Asp Val Val Cys Ile 280 Gly Leu Ile Ile His Glu Gly Pro Ser Val Tyr Arg Ile Phe Lys Arg 295 Trp Gln Ala Val Asn Gln Gln Trp Lys Val Leu Asn Tyr Asp Lys Thr 315 Lys Asp Leu Glu Asp Gln Lys Ala Gly Gly Arg Thr Asn Pro Arg Thr 330 Ser Ser Ser Thr Gln Ala Asn Ile Pro Ser Ser Glu Glu Glu Thr Ala 345 Gly Thr Pro Ala Pro Glu Gln Gly Pro Ala Gln Ala Ala Gly His Pro 360 Ser Gly Pro Leu Ser His His His Cys Ala Tyr Thr Ile Leu His Ile Leu Ser His Leu Arg Pro His Glu Gln Arg Ser Pro Pro Gly Ser Ser 395 Arg Glu Leu Val Met Arg Val Thr Thr Val

<210> 45

<211> 3666

<212> DNA

<213> Homo sapiens

<400> 45

aagacaagta ttcctgaaat gtgtcacctg gctctgttgg ccaagccagc agtgccacaa 60 gagaagcagc tgccatggcc cagtgacacc tggagtgttt gacgatgctt tgtgtccatg 120

```
tggcccctaa ccaggccttt ctcacagcca catagcatcc ccaggcctgc tgcactgggc 180
cagccgcage ctccgagece agectgaggg geeteteact gggatececa getttgteee 240
tgagatgagg gggctgatcc taagagtgtg ggtggggatg cctctgccca gggggttctg 300
gtggtgttgg gctctggccc aggcctcctg gctctgtgtc cttccataga ctccaggttc 360
ctcacagtca ttcacaaacc aactgaatgt tggtgtcttg tggcttctgg tctcagggtt 420
ggaggtatta aagccatgga agagcagtct ctcctgggct gcaacagcct gtcttctgtg 480
geetetaget ecateeteag agtttgggat aggggetgaa tettttgett gtteteeete 540
ccagggctgg cccccagagt cagtacttca ggttgagggg agtgggaggt tggctctgga 600
ggggctgccg agtggcagga ggaaggggct caggagcagg gggtggctcc actgcagcgg 660
ccagactctg ttgattacag atgattattt caaggtgtgt gtgtgtgtgc gcgtgtgtgt 720
gtgtgcgtgt gtgtattttt aaataacagc tctattgaga tatagttcac ataccataca 780
attcacccat tgaaagtgta caattcaatg gtttctagta tgttcacaga gttgtataat 840
gaacaccaca gttaatttta gaacattttc ttctattctc ttacaatgtg taaaaataaa 900
taaaggtttt tttaaaaaaa cattttcatc acaccaaaaa tgagctcctc gatggatgtt 960
atccctcatt tgtccccaaa cccccagccc ctggcaacca ctaatctact ttctatctct 1020
ggatttgcct atcatggaca tttcttatga acggagtgac acaccatgtg gcattttgtg 1080
tctggtttct tccactgagc atcatgattt caagttcatg taggagcatg catctgagct 1140
tcattccttc tcatggtgca atcatcttcc actgtgtgta taagaccaca ttttgtcaat 1200
ccacacatcc atggatcaca agtgcatttt taaagggtgc ttttacatct caaacacagt 1260
tctcagttgg cgagggggtc agaggacaat acagaagtga ctgtaagcgg cataaactgt 1320
agetteccag aggggeteca ggggeteggg ggagaggteg aggtagggag geaatgteet 1380
tcctttgagc agccactgag agggagaagg agttgcagag atcaggaagg agaggattta 1440
tttccagttt tctggcagtt tttcctcact ctttcggaga cctaggatgg gttaggagag 1500
ggcatggcaa aggcagaggt ggctctgcta gaggaggccg caggtccgca ggccgaacct 1560
ggggagccag ccatgtctgg cctgaggccc tgctttgagg agaagataaa gccttgagga 1620
gccttttggg ccgatctggg aacccagcaa gactagatta gcctgactga tgacagacct 1680
gggatgagga tgagggcagt taagtatttg tttaatcttg ctttgtcttt tcaaacagcg 1740
atttagtaat cetgtttgag getgeagtgt ggeaatgett teeagaggat ggagteettt 1800
ttgtttgttt tgaaaaaata gagataaggt ttcactatgt tgcctaggct ggtctcatac 1860
teggeeteaa geeateetee tgeetgggee teecaaagtg ttgggattae aggegtgage 1920
catggtgcca gactggagtc cttttattaa aattaactgc cctgctcagc tttctgctgg 1980
gccaccccag agccaatcct tggttcttgg gcccaaggct ggacccaggg gttgcaggaa 2040
acagtetgta geatecaagt ggggeetgte gtacceaete cagtgtgtag gtgcagaaeg 2100
ctctttgggg gatttctctg ctgggccacc ttactccagg gatccctcag ttttcaaaac 2160
aaagcaagag ggcaaggaag aatggagaaa cageteagtg ttgaetetet teeceetggt 2220
gagtgctgtg ctggggcctc tgtgcacatc ataccacttc ccccttgaat cagccccaca 2280
aggcagggtg agagatgagg actcagggtg caaggaggtc tcacagcttg gaaatggatc 2340
aggacagete tgatteteca aggeeaaggt ettetetata teatgaggea geecaaaaat 2400
agcgggaagg tgctttccag tgtgtatcag tgtggcccat ctgggagtca taatgtcatt 2520
gcctcttcca aaatatcagc aaagctgacc ctagtgcttg tagtgctcaa atgcacctct 2580
ctgcctttgt gccataggga aatggatttg gtcctggggg tggtgatacc aacttctgtc 2640
tcaattccat gaccctcact cagcaccccc accccaggcc tgtgcagagg aggaataacc 2700
gtccttgaga accatccagc cctaggtgga gaaattagat ttatggactt aatcagttct 2760
tottccctgt cagtggtggt gagaatgaaa tgggggaaat tgataagcct cagtcatgtt 2820
ttcctgcgag acaaggcagc tttggtagct ggtgggactg acgccttctt cacctgtgtc 2880
ctctgcctct gagtgactat aaattgcgaa ccccatgagg tggcacctgc agccacagat 2940
cgcttaggca ccttgcacag gggccaccta atgaactggc tgcaggacgg caatcctgcc 3000
gtgaagccag gcacctcggg aggggcaagg tggcagaacc gagagagcag atgctccttg 3060
ctgtttctgt aaggccacca gtggctgggt ggcctggccc tggtagcaag gtggtaaccg 3120
tgtgagtggc tgaatcctgc accacttttc ctgagcctcc ttcctcctgg attcctgcaa 3180
ctatattete actacatgge teaceaceaa ttegttetet etgeeceaag gaggetggae 3240
aagaggetea ggteagtgeg ggtaegeagg aacetatgte tgtaaaatga aaatgeetge 3300
cttcaagggc tgtcttgagg ttgaaaggag atggtctaca tcaagggtta ggaagaccac 3360
aatgtggctg tgccggccac ctccaggctg gcttcagtct cccatcccca tagtcatacc 3420
cctgtgaagt cccttcccat actgaatcgg gctacctgtg tatcttatag ggtgttggaa 3480
atgacagatt gtgaatteca aggeeecata aaagacageg tgggetggge gtggtggete 3540
acgcctgtaa tcccagcact ttgggaggcc gagccaagtg gatcacttga ggtcaggagt 3600
tctagaccag cctggccagc atggtgaaaa cctatctcta ctaaaaaaaa aaaaaaaaa 3660
aaaaaa
                                                                 3666
```

```
<210> 46
<211> 143
<212> PRT
<213> Homo sapiens
<400> 46
Met Val Pro Asp Trp Ser Pro Phe Ile Lys Ile Asn Cys Pro Ala Gln
Leu Ser Ala Gly Pro Pro Gln Ser Gln Ser Leu Val Leu Gly Pro Lys
                                 25
Ala Gly Pro Arg Gly Cys Arg Lys Gln Ser Val Ala Ser Lys Trp Gly
                             40
Leu Ser Tyr Pro Leu Gln Cys Val Gly Ala Glu Arg Ser Leu Gly Asp
Phe Ser Ala Gly Pro Pro Tyr Ser Arg Asp Pro Ser Val Phe Lys Thr
                     70
Lys Gln Glu Gly Lys Glu Glu Trp Arg Asn Ser Ser Val Leu Thr Leu
Phe Pro Leu Val Ser Ala Val Leu Gly Pro Leu Cys Thr Ser Tyr His
            100
                                105
Phe Pro Leu Glu Ser Ala Pro Gln Gly Arg Val Arg Asp Glu Asp Ser
Gly Cys Lys Glu Val Ser Gln Leu Gly Asn Gly Ser Gly Gln Leu
    130
                        135
<210> 47
<211> 2052
<212> DNA
<213> Homo sapiens
<400> 47
gactgtggtc gggagtaggc agcggcgccg cgtccgctct cgcccgctct cgcccgctcg 60
ccagccggct ctcctcccgc cgcaggaccc gcgcgccgcg ctcgggggcc atgcagcgcc 120
tggccatgga cctgcggatg ttgtcccggg agctctccct ctacctggaa caccaagtcc 180
gggtggggtt cttcggctcg ggggtgggct tatcccttat cctgggcttc agcgtcgctt 240
atgeetteta etaeetgage ageattgeea agaaaceeca gttagtgace gggggtgaga 300
gtttcagccg cttccttcaa gaccactgtc ccgtggttac agaaacgtac tacccgacgg 360
totggtgotg ggagggtoga ggacagacco tgottagaco tttcatcact togaagcoco 420
cggtgcagta caggaatgaa cttattaaaa ctgcagatgg aggacagatt tcactggact 480
ggtttgataa tgataacagt acgtgttata tggatgccag caccagacct actatcttat 540
tgttgcctgg cctcacggga acaagcaagg agtcatatat ccttcatatg atccatctta 600
gtgaagaatt aggatacaga tgtgtggttt ttaacaacag aggagtggcg ggggagaatc 660
tettgaegee aaggaettat tgttgtgeta acaetgaaga ettggagaea gttatteace 720
atgtacacag cotgtaccot totgotoott tootggcagc aggggtttca atgggaggaa 780
tgctgcttct aaattacttg ggcaaaattg ggtccaaaac gcctttgatg gcagctgcaa 840
ctttttccgt tggttggaac accttcgctt gctcagagtc attggaaaaa ccactgaact 900
ggctactttt taattactat ttgacaacct gccttcagtc ttcagttaat aagcaccgac 960
atatgtttgt aaaacaagtt gatatggatc atgtcatgaa ggctaaatcc atcagagagt 1020
ttgataagcg attcacttca gtcatgtttg gataccaaac aattgatgat tattatactg 1080
atgccagtcc gagtcctaga ctgaagtcag taggaattcc agtattgtgt ctaaattctg 1140
```

```
tggatgatgt tttctcaccc agtcatgcta ttccaataga aactgctaag caaaatccta 1200
atgttgcttt ggtccttact tcttatggag gccatattgg ttttctggag ggaatctggc 1260
 caagacagtc cacttacatg gatcgtgtct tcaagcaatt tgtgcaagcc atggttgagc 1320
atggacatga actetettaa catgtagtte tttgggtgca ttttgtetga accaeaattg 1380
tgaaggcagc tcagcttagt gcacaaattt taactgttgt atataaagca aataagccag 1440
ctttgtagca acaaattaaa tatagtatta gattgttact tacgtagatt ttattttac 1560
tatgccttac caagtacatc cttaaacaaa gtagtatgta catgaaattg cacttaacca 1620
aaactattgt gtaaaacaaa ttttaattcc tcagggtttt aatttaaact agtattttt 1680
tagattattt gttttaggtg atttaatggt actttaataa ctactaagaa atattggcta 1740
tttcaatgta agttataagg tggtacattc ctaagggtat ttatagttga tgataacatg 1800
aaaactgaaa taagataaaa tacaacgtgc taaatctttt atgtattcta actttaaaag 1860
acaagtgcaa caaagttaga ctgacttcta tatgtgctct tttactctga taatattaaa 1920
ttaggactaa cttatgtttt ataatgatta taatttacat gcttattttt aaaatagtat 1980
aaaaaaaaa aa
<210> 48
<211> 409
<212> PRT
<213> Homo sapiens
Met Gln Arg Leu Ala Met Asp Leu Arg Met Leu Ser Arg Glu Leu Ser
Leu Tyr Leu Glu His Gln Val Arg Val Gly Phe Phe Gly Ser Gly Val
Gly Leu Ser Leu Ile Leu Gly Phe Ser Val Ala Tyr Ala Phe Tyr Tyr
Leu Ser Ser Ile Ala Lys Lys Pro Gln Leu Val Thr Gly Gly Glu Ser
                       55
Phe Ser Arg Phe Leu Gln Asp His Cys Pro Val Val Thr Glu Thr Tyr
                   70
Tyr Pro Thr Val Trp Cys Trp Glu Gly Arg Gly Gln Thr Leu Leu Arg
Pro Phe Ile Thr Ser Lys Pro Pro Val Gln Tyr Arg Asn Glu Leu Ile
                              105
Lys Thr Ala Asp Gly Gly Gln Ile Ser Leu Asp Trp Phe Asp Asn Asp
Asn Ser Thr Cys Tyr Met Asp Ala Ser Thr Arg Pro Thr Ile Leu Leu
                      135
Leu Pro Gly Leu Thr Gly Thr Ser Lys Glu Ser Tyr Ile Leu His Met
                  150
                                     155
Ile His Leu Ser Glu Glu Leu Gly Tyr Arg Cys Val Val Phe Asn Asn
Arg Gly Val Ala Gly Glu Asn Leu Leu Thr Pro Arg Thr Tyr Cys Cys
                             185
                                                190
Ala Asn Thr Glu Asp Leu Glu Thr Val Ile His His Val His Ser Leu
```

195 200 205 Tyr Pro Ser Ala Pro Phe Leu Ala Ala Gly Val Ser Met Gly Gly Met 215 Leu Leu Asn Tyr Leu Gly Lys Ile Gly Ser Lys Thr Pro Leu Met 235 Ala Ala Ala Thr Phe Ser Val Gly Trp Asn Thr Phe Ala Cys Ser Glu 250 Ser Leu Glu Lys Pro Leu Asn Trp Leu Leu Phe Asn Tyr Tyr Leu Thr 265 Thr Cys Leu Gln Ser Ser Val Asn Lys His Arg His Met Phe Val Lys 280 Gln Val Asp Met Asp His Val Met Lys Ala Lys Ser Ile Arg Glu Phe 295 Asp Lys Arg Phe Thr Ser Val Met Phe Gly Tyr Gln Thr Ile Asp Asp 310 Tyr Tyr Thr Asp Ala Ser Pro Ser Pro Arg Leu Lys Ser Val Gly Ile 325 Pro Val Leu Cys Leu Asn Ser Val Asp Asp Val Phe Ser Pro Ser His 345 Ala Ile Pro Ile Glu Thr Ala Lys Gln Asn Pro Asn Val Ala Leu Val 360 Leu Thr Ser Tyr Gly Gly His Ile Gly Phe Leu Glu Gly Ile Trp Pro 375 Arg Gln Ser Thr Tyr Met Asp Arg Val Phe Lys Gln Phe Val Gln Ala 390 395 Met Val Glu His Gly His Glu Leu Ser 405 <210> 49 <211> 2505 <212> DNA <213> Homo sapiens <400> 49 ggacaggagg ctcaaggggg cggaggcggc gttgccgggc tctccggaag gagacgtggc 60

ggcggttggg ccggtgatac ccgggcgct tatagtccg ccgcctctc ctccactcc 120 cctctcctcc cctccctcc tggagcagag gaggttgtgg cggtggtgg agaaagcggc 180 ggcggaggaga ggagaagga ggcggcgcg tacggagtt ggtcccgggc ggtcccgggc gggccggtgt 240 ctggaggacat ccttctcca cttggagcgc ccggcggcg ccgagcctt cctcaactca 300 gcgatgacat ccctttccga gtcaactggc ccggcaccga gttctctctg cccacaactg 360 gagttttata taaagaagat aattatgtca tcatgacaac tgcacataaa gaaaatata 420 aatgatcaact tccccttgtg acaagtgggg ataggagaaga agaaaaggat tataaaggcc 480 ctaatccaag agagcttttg gaccactat ttaaacaaag cagttgttcc tacagaaata 420 aatgatctattg gacttactga gtatgtcatg gaaaacacat tcggcagtac catgaagaga 600 accttctatt tgaaaaagaa cgagaagcag aagaaaagga aaaatcaaat gagattccca 720

```
ctaaaaatat cgaaggtcag atgacaccat actatcctgt gggaatggga aatggtacac 780
 cttgtagttt gaaacagaac cggcccagat caagtactgt gatgtacata tgtcatcctg 840
 aatctaagca tgaaattctt tcagtagctg aagttacaac ttgtgaatat gaagttgtca 900
 ttttgacacc actcttgtgc agtcatccta aatataggtt cagagcatct cctgtgaatg 960
acatattttg tcaatcactg ccaggatctc catttaagcc cctcaccctg aggcagctgg 1020
agcagcagga agaaatacta agggtgcctt ttaggagaaa taaagaggaa gatttgcaat 1080
caactaaaga agagagattt ccagcgatcc acaagtcgat tgctattggc tctcagccag 1140
 tgctcactgt tgggacaacc cacatatcca aattgacaga tgaccaactc ataaaagagt 1200
ttettagtgg ttettactge tttegtgggg gtgteggttg gtggaaatat gaattetget 1260
atggcaaaca tgtacatcaa taccatgagg acaaggatag tgggaaaacc tctgtggttg 1320
 tegggacatg gaaccaagaa gagcatattg aatgggetaa gaagaataet getagagett 1380
atcatcttca agacgatggt acccagacag tcaggatggt gtcacatttt tatggaaatg 1440
gagatatttg tgatataact gacaaaccaa gacaggtgac tgtaaaacta aagtgcaaag 1500
aatcagattc acctcatgct gttactgtat atatgctaga gcctcactcc tgtcaatata 1560
ttcttggggt tgaatctcca gtgatctgta aaatcttaga tacagcagat gaaaatggac 1620
ttctttctct ccccaactaa aggatattaa agttagggga aagaaaagat cattgaaagt 1680
catgataatt tetgteecac tgtgteteat tatagagtte teagecattg gacetettet 1740
aaaggatggt ataaaatgac totcaaccac tttgtgaata catatgtgta tataagaggt 1800
tattgataaa cttctgaggc agacatttgt ctcgcttttt ttcatttttg ttgtgtctta 1860
taaactgact gtttttcttt gcttggatac tgtgattcca aaataaatct catccaagca 1920
agttagagtc cagcctaatc aaatgtcata attgttgtac ctattgaaag tttttaaata 1980
atagatttat tatgtaaatt atagtatatg taagtagcta atgaagtaaa gatcatgaag 2040
aaagaaattg ataggtgtaa atgagagacc atgtaaaata tgtaaattct agtacctgaa 2100
atcettteaa eagattttta tatageaact getetetgea agtagttaaa etagaaactg 2160
ggcacatggt agaggeteae atgggagttg teeteaceet tgttaatete aagaaaetet 2220
tatttataat aggttgcttc tctctcagaa cttttatcta ttacttttt cttcttatga 2280
gtatgtttac tctcagagta tctatctgat gtagacagtt ggtgatgctt ctgagactca 2340
gaatggttta ctctaacaaa acactgtgct gtctatccct tgtacttgcc tactgtaata 2400
tggatttcac ttctgaacag tttacagcac aatatttatt ttaaagtgaa taaaatgtcc 2460
acaagcagtg ttgtcatgta aaaaaaaaa aaaaaaaaa aaaaa
<210> 50
<211> 483
<212> PRT
<213> Homo sapiens
<400> 50
Met Glu Glu Gly Gly Gly Val Arg Ser Leu Val Pro Gly Gly Pro
                                    10
Val Leu Leu Val Leu Cys Gly Leu Leu Glu Ala Ser Gly Gly Gly Arg
Ala Leu Pro Gln Leu Ser Asp Asp Ile Pro Phe Arg Val Asn Trp Pro
                             40
Gly Thr Glu Phe Ser Leu Pro Thr Thr Gly Val Leu Tyr Lys Glu Asp
Asn Tyr Val Ile Met Thr Thr Ala His Lys Glu Lys Tyr Lys Cys Ile
                    70
Leu Pro Leu Val Thr Ser Gly Asp Glu Glu Glu Lys Asp Tyr Lys
Gly Pro Asn Pro Arg Glu Leu Leu Glu Pro Leu Phe Lys Gln Ser Ser
                                105
Cys Ser Tyr Arg Ile Glu Ser Tyr Trp Thr Tyr Glu Val Cys His Gly
       115
                           120
```

Lys	His 130	Ile	Arg	Gln	Tyr	His 135		Glu	Lys	Glu	Thr 140		Gln	Lys	Ile
Asn 145	Ile	His	Glu	Tyr	Туr 150	Leu	Gly	Asn	Met	Leu 155		Lys	Asn	Leu	Lev 160
Phe	Glu	Lys	Glu	Arg 165	Glu	Ala	Glu	Glu	Lys 170	Glu	Lys	Ser	Asn	Glu 175	
Pro	Thr	Lys	Asn 180	Ile	Glu	Gly	Gln	Met 185	Thr	Pro	Tyr	Tyr	Pro 190	Val	Gly
Met	Gly	Asn 195	Gly	Thr	Pro	Cys	Ser 200	Leu	Lys	Gln	Asn	Arg 205	Pro	Arg	Ser
Ser	Thr 210	Val	Met	Tyr	Ile	Cys 215	His	Pro	Glu	Ser	Lys 220	His	Glu	Ile	Leu
Ser 225	Val	Ala	Glu	Val	Thr 230	Thr	Cys	Glu	Tyr	Glu 235	Val	Val	Ile	Leu	Thr 240
Pro	Leu	Leu	Cys	Ser 2 <b>4</b> 5	His	Pro	Lys	туг	Arg 250	Phe	Arg	Ala	Ser	Pro 255	Val
Asn	Asp	Ile	Phe 260	Cys	Gln	Ser	Leu	Pro 265	Gly	Ser	Pro	Phe	Lys 270	Pro	Leu
Thr	Leu	Arg 275	Gln	Leu	Glu	Gln	Gln 280	Glu	Glu	Ile	Leu	Arg 285	Val	Pro	Phe
Arg	Arg 290	Asn	Lys	Glu	Glu	Asp 295	Leu	Gln	Ser	Thr	Lys 300	Glu	Glu	Arg	Phe
Pro 305	Ala	Ile	His	Lys	Ser 310	Ile	Ala	Ile	Gly	Ser 315	Gln	Pro	Val	Leu	Thr 320
Val	Gly	Thr	Thr	His 325	Ile	Ser	Lys	Leu	Thr 330	Asp	Asp	Gln	Leu	11e 335	Lys
Glu	Phe	Leu	Ser 340	Gly	Ser	Tyr	Cys	Phe 345	Arg	Gly	Gly	Val	Gly 350	Trp	Trp
Lys	Tyr	Glu 355	Phe	Cys	Tyr	Gly	Lys 360	His	Val	His	Gln	Tyr 365	His	Glu	Asp
Lys	Asp 370	Ser	Gly	Lys	Thr	Ser 375	Val	Val	Val	Gly	Thr 380	Trp	Asn	Gln	Glu
Glu 385	His	Ile	Glu	Trp	Ala 390	Lys	Lys	Asn	Thr	Ala 395	Arg	Ala	Tyr	His	Leu 400
Gln	Asp	qaA	Gly	Thr 405	Gln	Thr	Val	Arg	Met 410	Val	Ser	His	Phe	Tyr 415	Gly
Asn	Gly	Asp	11e 420	Cys	Asp	Ile	Thr	Asp 425	Lys	Pro	Arg	Gln	Val 430	Thr	Val
Lys	Leu	Lys 435	Cys	Lys	Glu	Ser	Asp 440	Ser	Pro	His	Ala	Val 445	Thr	Val	Tyr

```
Met Leu Glu Pro His Ser Cys Gln Tyr Ile Leu Gly Val Glu Ser Pro
       Val Ile Cys Lys Ile Leu Asp Thr Ala Asp Glu Asn Gly Leu Leu Ser
       465
                           470
                                               475
       Leu Pro Asn
       <210> 51
       <211> 2986
       <212> DNA
       <213> Homo sapiens
       <400> 51
       atgggagacc ctcgatgtgc agagccttcc cctgggagaa ggagctgaaa gacaaacacc 60
       ccagcttgtt ccaggcattg ctggagatgg atctgctgac cgtgccaagg aaccaaaatg 120
      aatctgtatc agaaatcggt gggaagatat ttgagaaggc tgtaaagaga ctctctagca 180
      ttgatggtct tcaccaaatt agctctatcg tcccctttct gacggattcc agctgctgtg 240
      gataccataa agcatcctac taccttgcag tcttttatga gactggatta aatgttcctc 300
      gggatcagct gcagggcatg ttgtatagtt tggttggagg ccaggggagt gagaggctgt 360
      cttcaatgaa tcttgggtat aaacactacc agggtattga caactacccc ctggactggg 420
      aactgtcgta tgcctactac agcaacattg ccaccaagac accccttgac cagcacacac 480
      tgcaaggaga tcaggcatat gttgaaacaa ttagactaaa agatgatgaa atactcaagg 540
      tacaaaccaa agaagatgga gatgtcttta tgtggttgaa gcatgaagct acccgaggca 600
      atgcagcagc tcagcaacga ttggcccaga tgctgttctg ggggcagcaa ggtgtggcca 660
      agaatcccga agcagcaatt gagtggtacg ccaagggcgc cctggagacg gaggatcctg 720
      cgttaatcta tgactatgcc attgtgctat tcaagggtca aggagtaaaa aagaacagac 780
      ggcttgcctt agagctgatg aagaaagcag cttccaaggg attgcatcag gcagtcaatg 840
      gcctgggatg gtattaccac aaattcaaga aaaattacgc caaagcagca aagtactggt 900
      taaaagcaga agaaatgggg aacccagatg cgtcatacaa tcttggagtc ctgcatttgg 960
      atggcatctt ccctggagtt cctggaagga atcaaacttt agctggtgaa tatttccata 1020
      aggetgegea aggtggaeae atggaaggga eettgtggtg ttetetetae tatateaeag 1080
      gcaacctgga gacattccct agagatcctg agaaagctgt tgtatgggca aaacatgtag 1140
      ctgagaaaaa tggctacttg ggccatgtca tccgcaaagg cctcaatgcc tacctggaag 1200
      gttcatggca tgaagctttg ctgtattatg ttttagcagc agaaactgga attgaagtgt 1260
      cacagacaaa tttagcacac atctgtgagg agaggccaga cctggccagg agatacttgg 1320
      gtgttaactg tgtttggaga tactataatt tctctgtttt tcaaatcgat gctccttcct 1380
      ttgcatattt gaagatggga gacctttact actatggcca ccaaaaccag tcacaagacc 1440
      tggagttgtc tgtgcagatg tacgcccaag ccgccctgga tggagactcc cagggatttt 1500
      traacctggc cctgctaatc gaggaaggta cgataatccc acaccatatc ttggatttct 1560
      tggaaattga ctcaactctc cattctaata acatctccat tctccaggaa ctgtacgaaa 1620
      ggtgctggag ccacagtaac gaggagtcct tcagcccctg ctccttggcc tggctttacc 1680
      tgcacttgcg gcttctctgg ggtgctatcc tgcactcagc cctgatctac tttctgggaa 1740
      cetttetget atecatattg ategeetgga etgtgeagta tttccagtet gtetcageaa 1800
      gegatecece tecaagacea teccaggeet ecceagacae tgecaegtee actgeaagte 1860
      cagetgtgae tecagetgea gatgeetetg accaagacca geceacagta actaataace 1920
      cggagccacg tgggtgaact gtgcactcca gttctctcca gatgagagag aatcttttca 1980
      acagetggta ttgggaaget ggggeeaggg catgateetg ataaacacet taaatgtett 2040
      gtcaactgga tgcaaatttt gcaattggtg tcatttttt taaagtcaaa ttacaaggaa 2100
      gtacccagat caggcagtgg taataccaaa ggtcatcaaa cacatacaag gaacatcttg 2160
      atcatagggc atgtggggaa gtttactggg ccatcacaga cttttgttct agtgattgta 2220
      tgtattagga gtcatagcat gccctacggc agatctggat tcttatacac taagatgtgt 2280
cttaagaatc acagtgcgtg cttcatccct ttattgaaga acagaaaatt atgactactc 2340
      tacaaggtgg ataatatttt ggtacctgtg cttgccacag ccctgttcct caaagctgaa 2400
      ttgatagatt tctctttgac ttccaagacc tagcagttat aaggcacctt gaaataaatt 2460
      gtttgtgcct ggaaatgcag ggagggcaat agctttgtaa attggtttac atttttctcc 2520
      ttgaattttt ctagggtcct agtgcttccg aatcatttaa tggcattgtc ggatatcttt 2580
```

```
tacatttcaa ttgcaatcca tgaaattaca tttagaagat tcttagtact taactgtagt 2640
cttctccatg aattacacgt tagaatagac tggcagcaac ggaatatgca gcaagtaagc 2700
ctctagctta tagtttcatc cctacccctc atgcctgcgt gagtctgtac agggatatgt 2760
gtgtgtgtgt gtgtgtgtgt gtgttagaga ggaagaggaa gagcagaatg tctgtataca 2820
acatggctgc taaggtagtg aataaatcag taatgcaata ttgtgggtcc aaactactct 2880
aaaaaaaaa aaaaaaaaaa aaaaaaaaa aaaaaaa
<210> 52
<211> 640
<212> PRT
<213> Homo sapiens
<400> 52
Met Cys Arg Ala Phe Pro Trp Glu Lys Glu Leu Lys Asp Lys His Pro
Ser Leu Phe Gln Ala Leu Leu Glu Met Asp Leu Leu Thr Val Pro Arg
Asn Gln Asn Glu Ser Val Ser Glu Ile Gly Gly Lys Ile Phe Glu Lys
Ala Val Lys Arg Leu Ser Ser Ile Asp Gly Leu His Gln Ile Ser Ser
Ile Val Pro Phe Leu Thr Asp Ser Ser Cys Cys Gly Tyr His Lys Ala
Ser Tyr Tyr Leu Ala Val Phe Tyr Glu Thr Gly Leu Asn Val Pro Arg
Asp Gln Leu Gln Gly Met Leu Tyr Ser Leu Val Gly Gly Gln Gly Ser
           100
                              105
Glu Arg Leu Ser Ser Met Asn Leu Gly Tyr Lys His Tyr Gln Gly Ile
Asp Asn Tyr Pro Leu Asp Trp Glu Leu Ser Tyr Ala Tyr Tyr Ser Asn
                      135
Ile Ala Thr Lys Thr Pro Leu Asp Gln His Thr Leu Gln Gly Asp Gln
Ala Tyr Val Glu Thr Ile Arg Leu Lys Asp Asp Glu Ile Leu Lys Val
                                  170
Gln Thr Lys Glu Asp Gly Asp Val Phe Met Trp Leu Lys His Glu Ala
Thr Arg Gly Asn Ala Ala Ala Gln Gln Arg Leu Ala Gln Met Leu Phe
                          200
Trp Gly Gln Gln Gly Val Ala Lys Asn Pro Glu Ala Ala Ile Glu Trp
Tyr Ala Lys Gly Ala Leu Glu Thr Glu Asp Pro Ala Leu Ile Tyr Asp
                                     235
Tyr Ala Ile Val Leu Phe Lys Gly Gln Gly Val Lys Lys Asn Arg Arg
```

245 250 255 Leu Ala Leu Glu Leu Met Lys Lys Ala Ala Ser Lys Gly Leu His Gln 265 Ala Val Asn Gly Leu Gly Trp Tyr Tyr His Lys Phe Lys Lys Asn Tyr Ala Lys Ala Ala Lys Tyr Trp Leu Lys Ala Glu Glu Met Gly Asn Pro Asp Ala Ser Tyr Asn Leu Gly Val Leu His Leu Asp Gly Ile Phe Pro 315 Gly Val Pro Gly Arg Asn Gln Thr Leu Ala Gly Glu Tyr Phe His Lys 330 Ala Ala Gln Gly Gly His Met Glu Gly Thr Leu Trp Cys Ser Leu Tyr 345 Tyr Ile Thr Gly Asn Leu Glu Thr Phe Pro Arg Asp Pro Glu Lys Ala 360 Val Val Trp Ala Lys His Val Ala Glu Lys Asn Gly Tyr Leu Gly His Val Ile Arg Lys Gly Leu Asn Ala Tyr Leu Glu Gly Ser Trp His Glu 390 Ala Leu Leu Tyr Tyr Val Leu Ala Ala Glu Thr Gly Ile Glu Val Ser 410 Gln Thr Asn Leu Ala His Ile Cys Glu Glu Arg Pro Asp Leu Ala Arg 425 Arg Tyr Leu Gly Val Asn Cys Val Trp Arg Tyr Tyr Asn Phe Ser Val 440 Phe Gln Ile Asp Ala Pro Ser Phe Ala Tyr Leu Lys Met Gly Asp Leu 455 Tyr Tyr Tyr Gly His Gln Asn Gln Ser Gln Asp Leu Glu Leu Ser Val Gln Met Tyr Ala Gln Ala Ala Leu Asp Gly Asp Ser Gln Gly Phe Phe 490 Asn Leu Ala Leu Leu Ile Glu Glu Gly Thr Ile Ile Pro His His Ile 505 Leu Asp Phe Leu Glu Ile Asp Ser Thr Leu His Ser Asn Asn Ile Ser 520 Ile Leu Gln Glu Leu Tyr Glu Arg Cys Trp Ser His Ser Asn Glu Glu 535 Ser Phe Ser Pro Cys Ser Leu Ala Trp Leu Tyr Leu His Leu Arg Leu 550 555 Leu Trp Gly Ala Ile Leu His Ser Ala Leu Ile Tyr Phe Leu Gly Thr

```
565
                                    570
                                                         575
Phe Leu Leu Ser Ile Leu Ile Ala Trp Thr Val Gln Tyr Phe Gln Ser
                                585
Val Ser Ala Ser Asp Pro Pro Pro Arg Pro Ser Gln Ala Ser Pro Asp
Thr Ala Thr Ser Thr Ala Ser Pro Ala Val Thr Pro Ala Ala Asp Ala
                        615
Ser Asp Gln Asp Gln Pro Thr Val Thr Asn Asn Pro Glu Pro Arg Gly
                    630
                                        635
<210> 53
<211> 1908
<212> DNA
<213> Homo sapiens
<400> 53
gaactcaaga tggcggacga gagtgagaca gcagtgaagc cgccggcacc tccqctqccq 60
cagatgatgg aagggaacgg gaacggccat gagcactgca gcgattgcga gaatgaggag 120
gacaacaget acaacegggg gtaacgaaat ceteggagte caatteeegt ecageeteec 180
acaacctggg tctctggggt gcggggaagt caccgggagc ttagtctagc cccacctca 240
tgttcttatt ggctaagtca ctaggattct gcctggcgat tggttattgc ctttgtcatt 300
taccaagggt gggtgctctg gatattaagg gccggagacg ttcagtactt ttattatata 360
aaagttetat geagtgttee actegtgtge tteaggeeat teetgggaaa agageatgtt 420
ggacgatggt tttcgatggt acaacacagg acagtctagt aacagtacag ttcaaaggga 480
acgttactta tagacgtgtt gtttgaacaa cgtgactagc aataaacgaa tcataaaaca 540
tttcgcagca gttcaccctc agtgaggaaa ctcatcagac tatacaaact qtatqtataa 600
ttatattgta aaatatcact accagagaat cccaaaatat aaactcacct tataaaccta 660
tgtaattaac ggtatggtaa tgctttgatt tacatagttt ccattgctcc aaataatcca 720
taagtateet gaacgatata ttaatataat taagtetteg aacatetttg cettgttace 780
tttgcagagc agccccaggc ttcaagaaat gagcgatgtt gtttcttgga gagtatttgg 840
aatcctcggg ctccatactg cctatcctgt actttagggt cttgccatta gttactattt 900
gttcctaggg atgaagaaac acaccaggca tttgaatgtt gaattctttt cccaaattag 960
tttttacttc tgtaagccac agcttattca tctttcttca catggttagt gcctggcact 1020
ggcactcacg ctgtctctcc ccatcttcct gtctatattt gtagatatat ttttaaactg 1080
aaagtcgtga gagatttttg ggtgtataac ttgctgagtc tgaggtagtc tgattttcqt 1140
agccagcttg ttattcgcag tattggtggc agtgcagata taaaggtata aagaccaagg 1200
actgcgtaga agagatggtc ccacaagatt atagtacata tttttattgt atcctttcta 1260
tgtttaggta tgcttagata cacaaatact taccattgta ttatagttgc ctgcagtact 1320
cagtaacatg cagcagccta ttgctcctag gctacaaacc tgtatagcat gttactgtaa 1380
tgtacaccat atagcctagg catttagtag gttataccat ctagatttgt gtaagtacac 1440
cctataatgt tggcaaggca aaaatcacct aaccatgcat ttcccagcac atatgcctga 1500
cgttcagtga agcatgactg tatttaagtg gtttataatc tgcttgtggt aaatcttagg 1560
ttaaaaagatc tagcttttat gttcttcagc cggcattaaa aatcacagga agggccgggc 1620
atggtggctc atgcctgtaa tcccagtact ttgggaggca gatcacgagg tcaggagatc 1680
gagaccatee tggctaacac tgtgaaatee catetetaet aaaaatacaa aaaatttage 1740
cgggcgtggt ggcgggcgcc tgtagtccca actactcggg aggctaaggc aggagaatgg 1800
cgtgaaccca ggaggcagag cttgcagtga gctgagatca cgccactgca ctccagcctg 1860
ggcgacagag cgagactccg actcaaaaaa aaaaaaaaa aaaaaaaa
<210> 54
<211> 88
<212> PRT
<213> Homo sapiens
<400> 54
```

```
Met Phe Leu Leu Ala Lys Ser Leu Gly Phe Cys Leu Ala Ile Gly Tyr
                                     10
Cys Leu Cys His Leu Pro Arg Val Gly Ala Leu Asp Ile Lys Gly Arg
Arg Arg Ser Val Leu Leu Tyr Lys Ser Ser Met Gln Cys Ser Thr
                             40
Arg Val Leu Gln Ala Ile Pro Gly Lys Arg Ala Cys Trp Thr Met Val
Phe Asp Gly Thr Thr Gln Asp Ser Leu Val Thr Val Gln Phe Lys Gly
Asn Val Thr Tyr Arg Arg Val Val
<210> 55
<211> 2969
<212> DNA
<213> Homo sapiens
<400> 55
gagttgagag atggcggccg ccgcaggtag atcgctcctg ctgctcctct cctctcgggg 60
cggcggcggc gggggcgccg gcggctgcgg ggcgctgact gccggctgct tccctgggct 120
gggcgtcagc cgccaccggc agcagcagca ccaccggacg gtacaccaga ggatcgcttc 180
ctggcagaat ttgggagctg tttattgcag cactgttgtg ccctctgatg atgttacagt 240
ggtttatcaa aatgggttac ctgtgatatc tgtgaggcta ccatcccggc gtgaacgctg 300
tcagttcaca ctcaagccta tctctgactc tgttggtgta tttttacgac aactgcaaga 360
agaggatcgg ggaattgaca gagttgctat ctattcacca gatggtgttc gcgttgctgc 420
ttcaacagga atagacetee teeteettga tgacettaag etggteatta atgacettaac 480
ataccacgta cgaccaccaa aaagagacct cttaagtcat gaaaatgcag caacgctgaa 540
tgatgtaaag acattggtcc agcaactata caccacactg tgcattgagc agcaccagtt 600
aaacaaggaa agggagetta ttgaaagaet agaggatete aaagageage tggeteeeet 660
ggaaaaggta cgaattgaga ttagcagaaa agctgagaag aggaccactt tggtgctatg 720
gggtggcctt gcctacatgg ccacacagtt tggcattttg gcccggctta cctggtggga 780
atattcctgg gacatcatgg agccagtaac atacttcatc acttatggaa gtgccatggc 840
aatgtatgca tattttgtaa tgacacgcca ggaatatgtt tatccagaag ccagagacag 900
acaatactta ctatttttcc ataaaggagc caaaaagtca cgttttgacc tagagaaata 960
caatcaactc aaggatgcaa ttgctcaggc agaaatggac cttaagagac tgagagaccc 1020
attacaagta catctgcctc tccgacaaat tggtgaaaaa gattgatctg caaaaagcct 1080
ctgaatcctg gcagaaggaa cacctgtttg cctttttaat taaagcattg caggtggaag 1140
ctgggagcca tgtggggggt agagcgtttt tacctttaat tataaaacaa aaacagaaag 1200
gatctgaggg aagaagggaa tgttaaaacc tgaggatcag gcattgtgga atataagctc 1260
aaagggctta gtgaatattg tcttaaccaa gtatctcagt ttctggatga aaatgatgca 1320
gttatatagt tgagagattc ataaagagaa aacaatgctg ggggtgttcg tttcttgcat 1380
ettetttgca gagtcagcaa aagagtaaca caccagcace ccactcgact ctatttgttt 1440
ttaatttaac tgtccctatt tttgacatag gagtaaataa atatactaga aaagcaaatt 1500
ctcatgatat gctaaaatat cattagcatt tattttaaat tggacccagt ctctgcagag 1560
ttaccaggaa tettteette cagcatecet ttactgacca cetacetgta cetettqqtt 1620
acactttttt ttccatttga taattggaac caacttataa ctgtttaata attgacactt 1680
tagattatct cttaatacct tcttaaatgt ctatatatcc cagtgctctg gatcagtgtc 1740
taaaaatcac tggcaacact gcatgaggtt gttggttttg ttttgtttta ttaattagtc 1800
tttcacagga ggaataattg ccctccttta tatacttatc tattgataat cccctctccc 1860
tccagaacac aaatcagagg gaaagggggt gttcagctgt actaccaaat caggaagatg 1920
taaggtttac aaattggcta agaatcatgg ctctgtagcc atttcaacca gaataatttt 1980
attgctaatc tgctttgtgt gacagcattc caggccagcc agatgggact gccttgtctg 2040
gaggetttgt teatetegaa ggacacacac ttecacactg tttgtgagee eteceacete 2100
```

```
cacaacttca gttgtaaatc aagtgtgtgg atctcaaagg gtgcaattta tctttatata 2160
ggaatacatt totagggctt cottcaagcc cactotottc accotatttt ttottatott 2220
aaattgagag aaagagaatt aatcttatac tttgtcaaaa cattttctac catatttcca 2280
gatgacatct gcgcttgaag agtcaaagga atctgtgtct aatatcctgt ttttaactgc 2340
tgtaggggca ggatggaaag gatgatgggg gctgccacac cactgattgg ccttttcttt 2400
cacgtgattc atcettectc attgtggcaa ggagttettt etettettet teeteetttg 2460
ggatcattgt gtatgaaaag aaaaacttta aatgacaaac ccagactcca ggtgccttgc 2520
aaaggttgaa ggccagccag gattgctgct gctgctgcta ctcctgccaa cacccctttc 2580
attggcatga cggaatgaaa ggatgcatgt ctccacttcc tgaccctccg cccacttcct 2640
tctccctcca ccacccccag tcgtcagctc cttccctcat ttatttttgt taagttgtgt 2700
gaattatttt taacccattt atcctgtttg tgcatagggt ttttaagaag aaacagcaca 2760
gtgcaacgag caaatctttt tggggtgtgt gggaagcaag ggagggagga catggagaaa 2820
agttctttaa acaaatagca aactattgaa catgtgtaaa atcctgtatc atttatgaaa 2880
tatgtataaa aagcaatgta ccttctggaa caataaatac ttattcaatt tttgaaaaaa 2940
aaaaaaaaa aaaaaaaaa
<210> 56
<211> 351
<212> PRT
<213> Homo sapiens
<400> 56
Met Ala Ala Ala Gly Arg Ser Leu Leu Leu Leu Ser Ser Arg
Gly Gly Gly Gly Gly Ala Gly Gly Cys Gly Ala Leu Thr Ala Gly
Cys Phe Pro Gly Leu Gly Val Ser Arg His Arg Gln Gln His His
Arg Thr Val His Gln Arg Ile Ala Ser Trp Gln Asn Leu Gly Ala Val
Tyr Cys Ser Thr Val Val Pro Ser Asp Asp Val Thr Val Val Tyr Gln
 65
                     70
Asn Gly Leu Pro Val Ile Ser Val Arg Leu Pro Ser Arg Arg Glu Arg
                85
Cys Gln Phe Thr Leu Lys Pro Ile Ser Asp Ser Val Gly Val Phe Leu
Arg Gln Leu Gln Glu Glu Asp Arg Gly Ile Asp Arg Val Ala Ile Tyr
       115
                            120
Ser Pro Asp Gly Val Arg Val Ala Ala Ser Thr Gly Ile Asp Leu Leu
Leu Leu Asp Asp Phe Lys Leu Val Ile Asn Asp Leu Thr Tyr His Val
                   150
Arg Pro Pro Lys Arg Asp Leu Leu Ser His Glu Asn Ala Ala Thr Leu
                                   170
Asn Asp Val Lys Thr Leu Val Gln Gln Leu Tyr Thr Thr Leu Cys Ile
Glu Gln His Gln Leu Asn Lys Glu Arg Glu Leu Ile Glu Arg Leu Glu
                            200
```

```
Asp Leu Lys Glu Gln Leu Ala Pro Leu Glu Lys Val Arg Ile Glu Ile
                       215
Ser Arg Lys Ala Glu Lys Arg Thr Thr Leu Val Leu Trp Gly Gly Leu
                   230
                                       235
Ala Tyr Met Ala Thr Gln Phe Gly Ile Leu Ala Arg Leu Thr Trp Trp
Glu Tyr Ser Trp Asp Ile Met Glu Pro Val Thr Tyr Phe Ile Thr Tyr
Gly Ser Ala Met Ala Met Tyr Ala Tyr Phe Val Met Thr Arg Gln Glu
                           280
Tyr Val Tyr Pro Glu Ala Arg Asp Arg Gln Tyr Leu Leu Phe Phe His
                       295
Lys Gly Ala Lys Lys Ser Arg Phe Asp Leu Glu Lys Tyr Asn Gln Leu
305
                   310
                                       315
Lys Asp Ala Ile Ala Gln Ala Glu Met Asp Leu Lys Arg Leu Arg Asp
                                   330
Pro Leu Gln Val His Leu Pro Leu Arg Gln Ile Gly Glu Lys Asp
           340
                               345
<210> 57
<211> 1727
<212> DNA
<213> Homo sapiens
<400> 57
gggaagggca tccttgaggc acccgaatgg tccctcaggg tgcagggagg cagaagcctg 60
gccacagagg agcctcctaa ggcagcagct gcagcaagcg caccctctcc ccactctccc 120
cacgccagag cggcttccag agcagatgct gtttccatcc tcctcgtcaa aaccattctc 180
getgetgage ttgacaatet gggcaagget tgtggggege ttgacaaaca gaatetgeee 240
tgtgccgcct ggttccgtgg cctccagcat gagcctgcag gcagggcgct gcgggaaccc 300
agttgtgctg ccccagccca tgcctccggg tctgctgtgc atgaatgagt gctcacttgt 360
cccgggttta ggacgtggtc aagtgaacag cagggtctaa ctgtgcttac ttagcccagt 420
tcaaacagaa caaaggaaaa atatagaaag caacatctgt tgatcattta ggtttttttt 480
taaaccacca tgtcactttg agtccttcat gggtttttga acagcattta tcaagaagaa 540
aatgtggget ttttcccctc tcccgtgttt tgtttgtcct gtagatagag ggaggaaagc 600
cgtgcagtgg caggcgggac cccctctggt ggcgggaccc cctcttgcgg tggtcttqcq 660
gggccagccg ggacctgtca ctttattatt taaggagtgt gtgtgtagag tcgctggctt 720
attaacagta tigigigigg gitigggitti tagittigitc citcilitig aagicccitc 780
atttcaatcc ttgactctct ctccccttcc cttgcccagc tctgttgaat gctgctgtgc 840
gcgtgtgagg gccgctctgc acacagggcc cttgggttgt gtgaactgaa attctccctg 900
tatttgtgag actcgcagga gtccccatct gtagcacagg caatgccagt gccatgctgc 960
agecteagaa accaggeete teactecage ageaggeaga accgtgtetg tggtegggtg 1020
ctgtccacag ctctgtctgc cttgttcttg ggcttgagct ggatagaggt ggggtctctt 1080
caccttccct gaattcagaa cagaccctgt gcctggcccc agtgtgccca ggcaattccc 1140
caggecetea ttgggageee ttggtgttet gageageagg geeeaggeag cacatgagea 1200
gtgcccaggg gctccctgcg tgaggacggc aaggtgcgat gtatgtctaa cttattgatg 1260
gcaggcagcc ccctgtgccc cctaagcctg gccctggtta ttgctgagct ctgtgctcag 1320
cagtetteae agacagaegt gagecaggeg gaggaetegt teettgeaga ggteagteet 1440
```

cacctgcagg tgtcggggtg gggggggca aggagggca ggcacacacc atgtctgacc 1500

```
tgaacccgat tetggggage atetteeege teeggeeeca egaceteeae agggttacat 1560
tgtaatatat atgccccage taacetgtet gatggtggca tetteetgca gacattteaa 1620
acatgtaact tttatatgaa aaaaaataaa cacagatgaa agctgaaaaa aaaaaaaaa 1680
<210> 58
<211> 115
<212> PRT
<213> Homo sapiens
<400> 58
Met Trp Ala Phe Ser Pro Leu Pro Cys Phe Val Cys Pro Val Asp Arg
Gly Arg Lys Ala Val Gln Trp Gln Ala Gly Pro Pro Leu Val Ala Gly
                               -25
Pro Pro Leu Ala Val Val Leu Arg Gly Gln Pro Gly Pro Val Thr Leu
Leu Phe Lys Glu Cys Val Cys Arg Val Ala Gly Leu Leu Thr Val Leu
Cys Val Gly Trp Val Phe Ser Leu Phe Leu Leu Phe Glu Val Pro Ser
                    70
Phe Gln Ser Leu Thr Leu Ser Pro Leu Pro Leu Pro Ser Ser Val Glu
                                    90
Cys Cys Cys Ala Arg Val Arg Ala Ala Leu His Thr Gly Pro Leu Gly
                               105
Cys Val Asn
       115
<210> 59
<211> 2617
<212> DNA
<213> Homo sapiens
<400> 59
tactgactcg aggggttccc ttccaaaata tgcagggctc aggctcccaa ttccgggcct 60
gtctgctttg cttgtgtttc tcctgtccct gttctcccgg agggcccagg tggaactcac 120
gacagggagg gagacgcttc ccaaaaacct gcagggctat ttcccagaat ttggttttca 180
agtacaaaac tttttgtcct gtaagatata tgcagcctca cagaagcagc ctctgcctcc 240
actttaccag ctacgtttt atcttaagca catggggctc ccttagaact tactccactg 300
atttaaaaaa aaaaaactg cctggcagca tctcagtgtc agagtgagca cggcacagga 360
aaggcccgtg gtgacgaggg tgaggtggcc acagtgaccg gacgacaaat gagactctgc 420
aaatgagact ccagagggtg aagatctgcg gtctccagac atcataggcc atgtgaccca 480
ctaggggccg cttacccctg gccgtccgct ggctgaactg aacgcattcc ctctctccgc 540
aacteteeeg tgaggetgea eeegtgtggg tageaetgga ageggeaetg tttgeattgt 600
acataggaag gaaggaagtt cttccagcct caccagcacc tggcagcgag tcagagcctg 660
tgagggcatc cgaagcagtg atgcagtgtc aacctcccag ctggtgccac tctgccctcg 720
ggggctccaa gcattgtaac tcagtcatgg gagctgcctc tttggaagtg cagatttatt 780
cctgtaataa tcctgcctgc ttttacctct cgtccactga ccagcaagtg tgagtcccgg 840
tgtcagtcgg cacagtccag tgtccatctg catttgctca tgcagagggg gtgagttggg 900
cactccctgt tgttggtttt ccttttgcag cacactgggc agtctcccta taaaacaaaa 960
accocacett etgtgeette tgetttagag cagagetece ceteccattt ceteagtett 1020
ccctgcaaaa tctgtccacc ggggaaggca gcaggaaccc tgggcagcgg gtgttctggg 1080
```

```
aaggctagtg acagcagatg tcatccagga acagccacac acggttctcc aggccgccgt 1140
cagcagctca aggtggggta tgagtgagaa gctgaggatc tcgcagcttg ttgctgagca 1200
aggtgcaacc gggctcatgc tgtcatcagc acaagacggg atggcaaggg ctttcagacg 1260
catttccaag agtccagcaa gccaggggga agatgatccc tttgccgaag tgtaccctct 1320
agccaacttt tgggagcgct tctgtttgca aagcgctggg gatgtgcctg tctctgtgtg 1380
acceacgaac gggaagggag agcactggag taatgacact tetgetgetg etttgattet 1440
caaggctgat ctttaaaacc ctcgccttgc tgacaggtgc tttaaaggca gtctgcatct 1500
tttcttccct tggtgtggga gaggtaaaca ctttgatttg ctgaaagctg tatggagtat 1560
atttgaacag ctagtagtta gctttgaaag tggaagtgtg aacagacact acttgtgtcg 1620
ctttgggtcc ttcactttac ccccacagaa gtctagaggc gtctgttata aagcgttacg 1680
gggcgcctgc atgcaggagg aaggacctgt attagctgga aatcatcagg aacccagctt 1740
geotecatet etetgagatg tgctgggtac ageotgeece tectagttet gtecaceggg 1800
aagagccggc tggcggcaga tccccagggg cagagcccct gctggatcct gggagctcat 1860
ctttacctgt gccggagtgg gaactgtgat tccagccggg caggtcagag tggagcagtg 1920
ctaagaggct gttgcaggag aactagacgg gcggggcctg ctgcatctgg atcatgtttc 1980
tgtgctctgc cccgcgctag ggactcaggg tctgggcttc tgccaggtga ggagcagaga 2040
gactgttccc ttgggtggag aggtgtgggc atgagagcca cccattgcca agcagcaaga 2100
atgttcgtgc ttttttccag agaggggaac cccactggtt tttgtggaaa caatggaaac 2160
ttacagatgc ctgcctggga tgatgaggca cattcagaac aaatgctttt ttttttttt 2220
agacagagte tegetetgae geceaggetg gagtgeagtg gegegatete ggeteaetge 2280
aaactttgcc tcccaggttc aagtgattct cctacctcag cctcccgagt agctgggatt 2340
acaccaccat gcccagcaaa tttttgtgtt tttagtagag acggagtttc accatgttgg 2400
ccaggetggt ctcgaactcc tgacctcagg tgatccatcc gccttggcct cccaaagtgc 2460
tgggattaca ggcgggagcc accatgcctg gccagaacaa atgccttttt aaacctttta 2520
agaacatttt taaaatgtct ttttctatgt caaatgtaac gtttattttt ttaaacaata 2580
aaattgattt gccaaaaaaa aaaaaaaa aaaaaaa
<210> 60
<211> 105
<212> PRT
<213> Homo sapiens
Met Gln Gly Ser Gly Ser Gln Phe Arg Ala Cys Leu Leu Cys Leu Cys
Phe Ser Cys Pro Cys Ser Pro Gly Gly Pro Arg Trp Asn Ser Arg Gln
                                 25
Gly Gly Arg Arg Phe Pro Lys Thr Cys Arg Ala Ile Ser Gln Asn Leu
Val Phe Lys Tyr Lys Thr Phe Cys Pro Val Arg Tyr Met Gln Pro His
                         55
Arg Ser Ser Leu Cys Leu His Phe Thr Ser Tyr Val Phe Ile Leu Ser
                     70
Thr Trp Gly Ser Leu Arg Thr Tyr Ser Thr Asp Leu Lys Lys Lys
Leu Pro Gly Ser Ile Ser Val Ser Glu
            100
<210> 61
<211> 1457
<212> DNA
<213> Homo sapiens
```

```
<400> 61
ttttttttg ctctcgctgg gaatggcgga gggagagaaa aaccaagatt tcactttcaa 60
gatggaaagt ccgtcagact cagctgtggt tttacctagc actcctcagg cctctgcgaa 120
tccatcatct ccctatacaa atagttcccg aaaacaacct atgagtgcaa cacttagaga 180
aagattaagg aaaacaagat tttcatttaa ttcctcttac aatgtggtga aacgtcttaa 240
agtagagagt gaagaaaatg atcagacctt ttcagagaaa ccagcatctt ccacagagga 300
aaactgtttg gaatttcaag aaagttttaa acatatagac agtgaatttg aagaaaatac 360
aaatttgaaa aatactttga agaatctcaa tgtctgtgaa tctcagtcac ttgattctgg 420
atcatgcagt gctctccaaa atgagtttgt gagtgagaag cttcctaaac aaagattaaa 480
cgctgaaaaa gccaaattgg tgaagcaggt tcaggagaaa gaagaccttc ttcggaggct 540
aaaactagtc aaaatgtata gatcaaagaa tgatctgtct cagttacagt tgttaataaa 600
gaagtggaga agctgtagcc agctcttgct ttatgagttg cagtcagctg tgtctgaaga 660
gaacaagaaa ctaagcetta etcaattgat agaceactat gggttagatg ataaattaet 720
acactataac agaagtgaag aagaatttat agatgtttaa ttcctgattt ttgctccaga 780
atatetttga gaatgacaac ttaattaaaa gataettagg caetttttt ttttttttga 840
gactgagttt cgctcttgtc atcctggctg gagtgtgatg gtgcgatctt gactcactgc 900
aacctetgee tetegggtte cagcaattet eetgeeteag eeteeegagt agetgagatt 960
acaggegeee gecaecatge eeggetaatt tttgeatttt tagtagagae tgggttteae 1020
cacgttggcc aggctggtct cgaactcctg acctcaggtg atccaccgcc taggcctccc 1080
aaaaccatta gggctcagag gaaggtatcc caatgaatat caattaaggg cactttaata 1140
tataaattat aaactaagtt ctaaaaggaa aattagtatt ttggatagat ttgtcaaaac 1200
gacatttaag tcatgtttaa aaagtcattt gggcagttct ggaaactagt tttaatacat 1260
ttgtttttta tgacaaaaag ttttatttta aatgttaaaa attgtccaat ctggtgaatg 1320
tctaacccta aagtttaaaa atttctgcct cctaagttta tgtaccttgt ttccatccat 1380
ttaccacata tttccatctg atagtctagc aggtaattaa acttatatgt ccaaaaaaaa 1440
aaaaaaaaa aaaaaaa
<210> 62
<211> 245
<212> PRT
<213> Homo sapiens
<400> 62
Met Ala Glu Gly Glu Lys Asn Gln Asp Phe Thr Phe Lys Met Glu Ser
                                     10
Pro Ser Asp Ser Ala Val Val Leu Pro Ser Thr Pro Gln Ala Ser Ala
                                 25
Asn Pro Ser Ser Pro Tyr Thr Asn Ser Ser Arg Lys Gln Pro Met Ser
                             40
Ala Thr Leu Arg Glu Arg Leu Arg Lys Thr Arg Phe Ser Phe Asn Ser
Ser Tyr Asn Val Val Lys Arg Leu Lys Val Glu Ser Glu Glu Asn Asp
                     70
Gln Thr Phe Ser Glu Lys Pro Ala Ser Ser Thr Glu Glu Asn Cys Leu
                                     90
Glu Phe Gln Glu Ser Phe Lys His Ile Asp Ser Glu Phe Glu Glu Asn
            100
                                105
Thr Asn Leu Lys Asn Thr Leu Lys Asn Leu Asn Val Cys Glu Ser Gln
                            120
Ser Leu Asp Ser Gly Ser Cys Ser Ala Leu Gln Asn Glu Phe Val Ser
   130
                        135
```

```
Glu Lys Leu Pro Lys Gln Arg Leu Asn Ala Glu Lys Ala Lys Leu Val
                                         155
Lys Gln Val Gln Glu Lys Glu Asp Leu Leu Arg Arg Leu Lys Leu Val
                                     170
Lys Met Tyr Arg Ser Lys Asn Asp Leu Ser Gln Leu Gln Leu Leu Ile
                                 185
Lys Lys Trp Arg Ser Cys Ser Gln Leu Leu Leu Tyr Glu Leu Gln Ser
                             200
Ala Val Ser Glu Glu Asn Lys Lys Leu Ser Leu Thr Gln Leu Ile Asp
                        215
His Tyr Gly Leu Asp Asp Lys Leu Leu His Tyr Asn Arg Ser Glu Glu
                    230
Glu Phe Ile Asp Val
                245
<210> 63
<211> 4093
<212> DNA
<213> Homo sapiens
<400> 63
tttgttccgg gagccgtcac cacagtaggt ccctcggctc agtcggccca gcccctctca 60
gteeteecea acceecacaa cegeeegegg etetgagaeg eggeeeegge ggeggeggea 120
gcagctgcag catcatctcc accetecage catggaagae etggaccagt etectetggt 180
etegteeteg gacageecae eeeggeegea geeegegtte aagtaceagt tegtgaggga 240
gcccgaggac gaggaggaag aagaggagga ggaagaggag gacgaggacg aagacctgga 300
ggagetggag gtgetggaga ggaageeege egeegggetg teegeggeee eagtgeeeae 360
egeceetgee geeggegege ceetgatgga etteggaaat gaettegtge egeeggegee 420
ccggggaccc ctgccggccg ctcccccgt cgccccggag cggcagccgt cttgggaccc 480
gageceggtg tegtegaceg tgecegegee atcecegetg tetgetgeeg cagtetegee 540
ctccaagctc cetgaggacg acgageetee ggcceggeet eccetteete ecceggecag 600
cytyagcccc caggcagagc ccgtgtggac cccgccagcc ccggctcccg ccgcgccccc 660
ctccaccccg gccgcgcca agcgcagggg ctcctcgggc tcagtggatg agaccctttt 720
tgetetteet getgeatetg ageetgtgat aegeteetet geagaaaata tggaettgaa 780
ggagcageca ggtaacacta ttteggetgg teaagaggat tteecatetg teetgettga 840
aactgetget tetetteett etetgtetee teteteagee gettettea aagaacatga 900
ataccttggt aatttgtcaa cagtattacc cactgaagga acacttcaag aaaatgtcag 960
tgaagcttct aaagaggtct cagagaaggc aaaactctac tcatagatag agatttaaca 1020
gagttttcag aattagaata ctcagaaatg ggatcatcgt tcagtgtctc tccaaaagca 1080
gaatctgccg taatagtagc aaatcctagg gaagaaataa tcgtgaaaaa taaagatgaa 1140
gaagagaagt tagttagtaa taacatcctt cataatcaac aagagttacc tacagctctt 1200
actaaattgg ttaaagagga tgaagttgtg tcttcagaaa aagcaaaaga cagttttaat 1260
gaaaagagag ttgcagtgga agctcctatg agggaggaat atgcagactt caaaccattt 1320
gagcgagtat gggaagtgaa agatagtaag gaagatagtg atatgttggc tgctggaggt 1380
aaaatcgaga gcaacttgga aagtaaagtg gataaaaaat gttttgcaga tagccttgag 1440
caaactaatc acgaaaaaga tagtgagagt agtaatgatg atacttettt ccccagtacg 1500
ccagaaggta taaaggatcg ttcaggagca tatatcacat gtgctccctt taacccagca 1560
gcaactgaga gcattgcaac aaacattttt cctttgttag gagatcctac ttcagaaaat 1620
aagaccgatg aaaaaaaaat agaagaaaag aaggcccaaa tagtaacaga gaagaatact 1680
agcaccaaaa catcaaaccc ttttcttgta gcagcacagg attctgagac agattatgtc 1740
acaacagata atttaacaaa ggtgactgag gaagtcgtgg caaacatgcc tgaaggcctg 1800
actccagatt tagtacagga agcatgtgaa agtgaattga atgaagttac tggtacaaag 1860
attgcttatg aaacaaaaat ggacttggtt caaacatcag aagttatgca agagtcactc 1920
```

```
tatcctgcag cacagetttg eccateattt gaagagteag aagetaetee tteaccagtt 1980
ttgcctgaca ttgttatgga agcaccattg aattctgcag ttcctagtgc tggtgcttcc 2040
gtgatacage ccageteate accattagaa gettetteag ttaattatga aagcataaaa 2100
catgageetg aaaaceeece accatatgaa gaggeeatga gtgtateact aaaaaaagta 2160
tcaggaataa aggaagaaat taaagagcct gaaaatatta atgcagctct tcaagaaaca 2220
gaageteett atatatetat tgeatgtgat ttaattaaag aaacaaaget ttetgetgaa 2280
ccagctccgg atttctctga ttattcagaa atggcaaaag ttgaacagcc agtgcctgat 2340
cattetgage tagttgaaga tteeteacet gattetgaae eagttgaett atttagtgat 2400
gattcaatac ctgacgttcc acaaaaacaa gatgaaactg tgatgcttgt gaaagaaagt 2460
ctcactgaga cttcatttga gtcaatgata gaatatgaaa ataaggaaaa actcagtgct 2520
ttgccacctg agggaggaaa gccatatttg gaatctttta agctcagttt agataacaca 2580
aaagataccc tgttacctga tgaagtttca acattgagca aaaaggagaa aattcctttg 2640
cagatggagg agctcagtac tgcagtttat tcaaatgatg acttatttat ttctaaggaa 2700
gcacagataa gagaaactga aacgttttca gattcatctc caattgaaat tatagatgag 2760
ttccctacat tgatcagttc taaaactgat tcattttcta aattagccag ggaatatact 2820
gacctagaag tatcccacaa aagtgaaatt gctaatgccc cggatggagc tgggtcattg 2880
ccttgcacag aattgcccca tgacctttct ttgaagaaca tacaacccaa agttgaagag 2940
aaaatcagtt teteagatga ettttetaaa aatgggtetg etacatcaaa ggtgetetta 3000
ttgcctccag atgtttctgc tttggccact caagcagaga tagagagcat agttaaaccc 3060
aaagttettg tgaaagaage tgagaaaaa etteetteeg atacagaaaa agaggacaga 3120
tcaccatctg ctatattttc agcagagctg agtaaaactt cagttgttga cctcctgtac 3180
tggagagaca ttaagaagac tggagtggtg tttggtgcca gcctattcct gctgctttca 3240
ttgacagtat tcagcattgt gagcgtaaca gcctacattg ccttggccct gctctctgtg 3300
accatcaget ttaggatata caagggtgtg atccaageta tecagaaate agatgaagge 3360
cacccattca gggcatatct ggaatctgaa gttgctatat ctgaggagtt ggttcagaag 3420
tacagtaatt ctgctcttgg tcatgtgaac tgcacgataa aggaactcag gcgcctcttc 3480
ttagttgatg atttagttga ttctctgaag tttgcagtgt tgatgtgggt atttacctat 3540
gttggtgcct tgtttaatgg tctgacacta ctgattttgg ctctcatttc actcttcagt 3600
gttcctgtta tttatgaacg gcatcaggca cagatagatc attatctagg acttgcaaat 3660
aagaatgtta aagatgctat ggctaaaatc caagcaaaaa tccctggatt gaagcgcaaa 3720
gctgaatgaa aacgcccaaa ataattagta ggagttcatc tttaaagggg atattcattt 3780
gattatacgg gggagggtca gggaagaacg aaccttgacg ttgcagtgca gtttcacaga 3840
togttgttag atotttattt ttagccatgo actgttgtga ggaaaaatta cotgtottga 3900
ctgccatgtg ttcatcatct taagtattgt aagctgctat gtatggattt aaaccgtaat 3960
catatetttt teetatetga ggeaetggtg gaataaaaaa eetgtatatt ttaetttgtt 4020
gcagatagtc ttgccgcatc ttggcaagtt gcagagatgg tggagctaga aaaaaaaaa 4080
aaaaaaaaa aaa
<210> 64
<211> 893
<212> PRT
<213> Homo sapiens
<400> 64
Met Gly Ser Ser Phe Ser Val Ser Pro Lys Ala Glu Ser Ala Val Ile
                                     10
Val Ala Asn Pro Arg Glu Glu Ile Ile Val Lys Asn Lys Asp Glu Glu
Glu Lys Leu Val Ser Asn Asn Ile Leu His Asn Gln Gln Glu Leu Pro
Thr Ala Leu Thr Lys Leu Val Lys Glu Asp Glu Val Val Ser Ser Glu
Lys Ala Lys Asp Ser Phe Asn Glu Lys Arg Val Ala Val Glu Ala Pro
                    70
                                         75
```

Met Arg Glu Glu Tyr Ala Asp Phe Lys Pro Phe Glu Arg Val Trp Glu

85 90 95

Val Lys Asp Ser Lys Glu Asp Ser Asp Met Leu Ala Ala Gly Gly Lys 100 105 110

Ile Glu Ser Asn Leu Glu Ser Lys Val Asp Lys Lys Cys Phe Ala Asp 115 120 125

Ser Leu Glu Gln Thr Asn His Glu Lys Asp Ser Glu Ser Ser Asn Asp 130 135 140

Asp Thr Ser Phe Pro Ser Thr Pro Glu Gly Ile Lys Asp Arg Ser Gly 145 150 155 160

Ala Tyr Ile Thr Cys Ala Pro Phe Asn Pro Ala Ala Thr Glu Ser Ile 165 170 170

Ala Thr Asn Ile Phe Pro Leu Leu Gly Asp Pro Thr Ser Glu Asn Lys 180 185 190

Thr Asp Glu Lys Lys Ile Glu Glu Lys Lys Ala Gln Ile Val Thr Glu 195 200 205

Lys Asn Thr Ser Thr Lys Thr Ser Asn Pro Phe Leu Val Ala Ala Gln 210 215 220

Asp Ser Glu Thr Asp Tyr Val Thr Thr Asp Asn Leu Thr Lys Val Thr 225 235 240

Glu Glu Val Val Ala Asn Met Pro Glu Gly Leu Thr Pro Asp Leu Val
245 250 255

Gln Glu Ala Cys Glu Ser Glu Leu Asn Glu Val Thr Gly Thr Lys Ile 260 265 270

Ala Tyr Glu Thr Lys Met Asp Leu Val Gln Thr Ser Glu Val Met Gln 275 280 285

Glu Ser Leu Tyr Pro Ala Ala Gln Leu Cys Pro Ser Phe Glu Glu Ser 290 295 300

Glu Ala Thr Pro Ser Pro Val Leu Pro Asp Ile Val Met Glu Ala Pro 305 310 315 320

Leu Asn Ser Ala Val Pro Ser Ala Gly Ala Ser Val Ile Gln Pro Ser 325 330 335

Ser Ser Pro Leu Glu Ala Ser Ser Val Asn Tyr Glu Ser Ile Lys His 340 345 350

Glu Pro Glu Asn Pro Pro Pro Tyr Glu Glu Ala Met Ser Val Ser Leu 355 360 365

Lys Lys Val Ser Gly Ile Lys Glu Glu Ile Lys Glu Pro Glu Asn Ile 370 375 380

Asn Ala Ala Leu Gln Glu Thr Glu Ala Pro Tyr Ile Ser Ile Ala Cys 385 390 395 400

Asp Leu Ile Lys Glu Thr Lys Leu Ser Ala Glu Pro Ala Pro Asp Phe

405 410 415 Ser Asp Tyr Ser Glu Met Ala Lys Val Glu Gln Pro Val Pro Asp His 425 Ser Glu Leu Val Glu Asp Ser Ser Pro Asp Ser Glu Pro Val Asp Leu Phe Ser Asp Asp Ser Ile Pro Asp Val Pro Gln Lys Gln Asp Glu Thr 455 460 Val Met Leu Val Lys Glu Ser Leu Thr Glu Thr Ser Phe Glu Ser Met 475 Ile Glu Tyr Glu Asn Lys Glu Lys Leu Ser Ala Leu Pro Pro Glu Gly 485 490 Gly Lys Pro Tyr Leu Glu Ser Phe Lys Leu Ser Leu Asp Asn Thr Lys 505 Asp Thr Leu Leu Pro Asp Glu Val Ser Thr Leu Ser Lys Lys Glu Lys 520 Ile Pro Leu Gln Met Glu Glu Leu Ser Thr Ala Val Tyr Ser Asn Asp 535 Asp Leu Phe Ile Ser Lys Glu Ala Gln Ile Arg Glu Thr Glu Thr Phe Ser Asp Ser Ser Pro Ile Glu Ile Ile Asp Glu Phe Pro Thr Leu Ile 570 Ser Ser Lys Thr Asp Ser Phe Ser Lys Leu Ala Arg Glu Tyr Thr Asp 580 585 Leu Glu Val Ser His Lys Ser Glu Ile Ala Asn Ala Pro Asp Gly Ala 600 Gly Ser Leu Pro Cys Thr Glu Leu Pro His Asp Leu Ser Leu Lys Asn 615 Ile Gln Pro Lys Val Glu Glu Lys Ile Ser Phe Ser Asp Asp Phe Ser Lys Asn Gly Ser Ala Thr Ser Lys Val Leu Leu Pro Pro Asp Val 650 Ser Ala Leu Ala Thr Gln Ala Glu Ile Glu Ser Ile Val Lys Pro Lys 665 Val Leu Val Lys Glu Ala Glu Lys Lys Leu Pro Ser Asp Thr Glu Lys 680 Glu Asp Arg Ser Pro Ser Ala Ile Phe Ser Ala Glu Leu Ser Lys Thr Ser Val Val Asp Leu Leu Tyr Trp Arg Asp Ile Lys Lys Thr Gly Val 705

710

Val Phe Gly Ala Ser Leu Phe Leu Leu Leu Ser Leu Thr Val Phe Ser

715

725 730 735 Ile Val Ser Val Thr Ala Tyr Ile Ala Leu Ala Leu Leu Ser Val Thr 745 Ile Ser Phe Arg Ile Tyr Lys Gly Val Ile Gln Ala Ile Gln Lys Ser 760 Asp Glu Gly His Pro Phe Arg Ala Tyr Leu Glu Ser Glu Val Ala Ile 775 780 Ser Glu Glu Leu Val Gln Lys Tyr Ser Asn Ser Ala Leu Gly His Val Asn Cys Thr Ile Lys Glu Leu Arg Arg Leu Phe Leu Val Asp Asp Leu 810 Val Asp Ser Leu Lys Phe Ala Val Leu Met Trp Val Phe Thr Tyr Val 825 Gly Ala Leu Phe Asn Gly Leu Thr Leu Leu Ile Leu Ala Leu Ile Ser 840 Leu Phe Ser Val Pro Val Ile Tyr Glu Arg His Gln Ala Gln Ile Asp 855 860 His Tyr Leu Gly Leu Ala Asn Lys Asn Val Lys Asp Ala Met Ala Lys 865 870 875 Ile Gln Ala Lys Ile Pro Gly Leu Lys Arg Lys Ala Glu <210> 65 <211> 3033 <212> DNA <213> Homo sapiens <400> 65 atacttcata gctgtggaag atgacaaaat tttaccatta aattcagctg aaaggaaacc 60 tggtgtgaag catgcaccat atataagcat tgcaggtgat gatcctcctg caagctgtgt 120 gtttagtcaa gttatgaaca tggcagcctt cctagccctt gtggtagctg ttctgcgctt 180 catacaactg aaaccgaagg ttttaaaccc gtggctgaat attagtggat tggtggctct 240 gtgtctggct tccttcggaa tgaccttact tggtaatttt cagctcacaa atgatgaaga 300 aatccataac gtcggaactt ccttgacctt tggatttggc acattgacct gctggatcca 360 ggctgcgctg acactcaagg tcaacatcaa gaatgaagga cggagagttg gaattccacg 420 ggttattctg tcggcatcta tcactctctg tgtggtcctc tacttcatcc tcatggccca 480 aagcatccac atgtatgcag ccagggtcca gtggggcctg gtcatgtgct tcctgtctta 540 ttttggcacc tttgccgtgg agttccggca ttaccgctat gagattgttt gctctgagta 600 ccaggagaat ttcctaagct tctcagaaag cctgtcagaa gcttctgaat atcagactga 660 ccaggtgtaa accatcagtt tttccttgct ggtgaggtgg gtgtgacagt gggggagggg 720 ccagtaggac acactcacag gacttgacat agaacctcat ttcacacaca cacacacac 780 cacattcatg gccacatttg ccaaatgagc ttttcagggc gagttatttc tttaatgaaa 840 aagcacaage eettatgtgt egaaatacae getgttacae tgaaaatata tgeaegacag 900 agcaagaage tigigeatga teaettetta teegteeeet teecageaet eeeteetett 960 cccattetet ccacatgtet caageaceet accgagtagg gcaggecaaa tgtteettgg 1020 gagtaatgcc aactcccgac gttgccttca ggtccaaagg gcttggaacc agctcgtgag 1080 gaagttetga atetggeact aatattettg agtggataat agtgtateat agaataggae 1140 ggaaattgta ttgagatgtg accetgtgte geetgtggaa aggeatagtg agaagaactt 1200 teccaegaaa geeeettea tegttgttea gtggtegget gtgtggatee caggagagae 1260

```
atatgccaca gactgtgaga gcaaagcccg ccgctgtgat ctggacttga tgcactgtga 1320
 ctgagaatga tttccaaatg tgaatatgtg tagggacgtg gtctatcagg cctggaacaa 1380
 gatgggggca gtgaaggtat ggtttagtgt ttgctttcat agtatgccat gtacaatgtt 1440
 ttatatttca tagtttcttt taagtaacta ccatgagtct ctctaagcct catggacaaa 1500
 gatgtagacc aaatgcaaga gctgagcttg ctttgggttc aaccatgatc aaagaaaaac 1560
 tgaggtcacc tgcaggctta cgtgggaagc taagaaaata tcacagaaaa atggaaagaa 1620
 atatggatgt gcagaggtaa taaaaagagc tgctgctgga catttatcaa agataggcac 1680
cttacagtat cttgttgcaa gtccaaatca ggggagactt tgttaatatg tatcttttgc 1740
tcaaatttag tagggttttt ttttttttg gattaagggc ttttcaaatt tggaatttgt 1800
agaagccaat taaaagaata cccttcctaa aaaccaaatt gacacagctg gccccctgc 1860
tagccaaccc gcagttccca gttcccacct gctgagagtt cagaactcag accgtaggtg 1920
tgggcttatg agactgtgct tcatgaagaa aagcagaatt ccaaattcaa actgttggag 1980
tgagccaagt ggacagaccc tccatgagtg cactttcttc caagaaatcc ccagatttac 2040
cccatagagg tctgggatta cctggaatat aatatgaaaa acattttta ggctgggtgt 2100
ggggeteaca cetgtaatee cageaetttg ggaggetgag gegggeggat cacetgaggt 2160
tgggagctcg agaccagcct gaccaatgtg aagaaacccc gtctctacta aaaaaaatac 2220
aaaattagee tggtgtggtg gegeatgeet gtaateeegg etaeteagga ggeggaggea 2280
ggagaatcac ttgaacccgg gaggcaggtt gcggtgagac gagatcacgc cattgcactc 2340
cagcctgggc aaaaagagct aaaaactcca tctcaaaaaa aaaaagaaaa aaagaaaaac 2400
gttttttaat tcaacccaaa gtctgaattt cttgaggaaa aggtcaatgt cttttcatct 2460
ctgtattgtt ccccacctct taacacagtg cctggcacat actaggtgct caataaatgt 2520
ctgttgaata gaattattaa taatttaaga gtaggaaaaa ggagtgtcag agagagactc 2580
aaagatgagt gagagagcat ggaagatggc tgtttcatgt gagacaggaa tggaagaagt 2640
tatgaatagg gatcagatgg gggagtgaga atccctgtaa gtaaaatgtg aggaaaagaa 2700
caagetgaga acaagattet eetgteaaaa aggegtetta etgtaaatag tecaaggtga 2760
catttgttag ttttgaatac tgcttttggg tttctttttt tcatttttat attttaaaat 2820
ttttatcaaa gaacaaagac ttatgtagtt ttcttttatt ctacacaatc caaattaaac 2880
agettttggt gatgcaattg tacactttct taagaatata tetaatacca cattttagca 2940
gaaccaagca atgactgaca ttattcattg ggatctggcc actaaataaa attctttat 3000
gcataaaaaa aaaaaaaaa aataaaaaaa aaa
<210> 66
<211> 178
<212> PRT
<213> Homo sapiens
<400> 66
Met Asn Met Ala Ala Phe Leu Ala Leu Val Val Ala Val Leu Arg Phe
                  5
Ile Gln Leu Lys Pro Lys Val Leu Asn Pro Trp Leu Asn Ile Ser Gly
Leu Val Ala Leu Cys Leu Ala Ser Phe Gly Met Thr Leu Leu Gly Asn
                             40
Phe Gln Leu Thr Asn Asp Glu Glu Ile His Asn Val Gly Thr Ser Leu
Thr Phe Gly Phe Gly Thr Leu Thr Cys Trp Ile Gln Ala Ala Leu Thr
                     70
Leu Lys Val Asn Ile Lys Asn Glu Gly Arg Arg Val Gly Ile Pro Arg
Val Ile Leu Ser Ala Ser Ile Thr Leu Cys Val Val Leu Tyr Phe Ile
Leu Met Ala Gln Ser Ile His Met Tyr Ala Ala Arg Val Gln Trp Gly
       115
                            120
```

```
Leu Val Met Cys Phe Leu Ser Tyr Phe Gly Thr Phe Ala Val Glu Phe
                          135
 Arg His Tyr Arg Tyr Glu Ile Val Cys Ser Glu Tyr Gln Glu Asn Phe
 145
                      150
                                          155
 Leu Ser Phe Ser Glu Ser Leu Ser Glu Ala Ser Glu Tyr Gln Thr Asp
                                      170
 Gln Val
 <210> 67
 <211> 504
 <212> DNA
 <213> Homo sapiens
 <400> 67
 aaaatccctg ctcccagctg ctttactaaa gagcaagttc ctgggcatct ctgtgtttct 60
 ctttatgggg ttcaaaacct ttcaaggacc tctctccatg ccactggttc cttggaccct 120
 atcactggge tgeeteetga geeceteagt cetaccacag tetactgaet ttteccatte 180
 agetgtgage atteaaccet gteecetgga cettgacace tggeteecca accetgteec 240
 aggaaaccca gattccacca gacacttcct tcttccccc gaggctatct ggcctgagac 300
 aacaaatgct gcctcccacc ctgagtctgg cactgggact ttcagaactc ctccttccct 360
 gactetttge eccagaceeg teatteaatg getagetttt teeatgggaa aaacaegage 420
 acceccaace acaaeggeea gttetetgat tecetaaate egeaceettt teaaaaecte 480
 aaaaaaaaa aaaaaaaaa aaaa
                                                                    504
 <210> 68
 <211> 130
 <212> PRT
 <213> Homo sapiens
 Met Gly Phe Lys Thr Phe Gln Gly Pro Leu Ser Met Pro Leu Val Pro
                   5
Trp Thr Leu Ser Leu Gly Cys Leu Leu Ser Pro Ser Val Leu Pro Gln
                                  25
 Ser Thr Asp Phe Ser His Ser Ala Val Ser Ile Gln Pro Cys Pro Leu
 Asp Leu Asp Thr Trp Leu Pro Asn Pro Val Pro Gly Asn Pro Asp Ser
      50
                          55
 Thr Arg His Phe Leu Leu Pro Pro Glu Ala Ile Trp Pro Glu Thr Thr
                      70
 Asn Ala Ala Ser His Pro Glu Ser Gly Thr Gly Thr Phe Arg Thr Pro
 Pro Ser Leu Thr Leu Cys Pro Arg Pro Val Ile Gln Trp Leu Ala Phe
             100
                                 105
 Ser Met Gly Lys Thr Arg Ala Pro Pro Thr Thr Thr Ala Ser Ser Leu
        115
                             120
                                                 125
```

```
Ile Pro
    130
 <210> 69
 <211> 3103
 <212> DNA
 <213> Homo sapiens
 <400> 69
 gatecgetge tettgtgacg ttgtggagat ggggagegte etggggetgt getecatgge 60
 gagetggata ceatgtttgt gtggaagtge ecegtgtttg etatgeegat getgteetag 120
 tggaaacaac tccactgtaa ctagattgat ctatgcactt ttcttgcttg ttggagtatg 180
 tgtagcttgt gtaatgttga taccaggaat ggaagaacaa ctgaataaga ttcctggatt 240
 ttgtgagaat gagaaaggtg ttgtcccttg taacattttg gttggctata aagctgtata 300
tegtttgtge tttggtttgg ctatgtteta tettettete tetttaetaa tgatcaaagt 360
gaagagtagc agtgatccta gagctgcagt gcacaatgga ttttggttct ttaaatttgc 420
tgcagcaatt gcaattatta ttggggcatt cttcattcca gaaggaactt ttacaactgt 480
gtggttttat gtaggcatgg caggtgcctt ttgtttcatc ctcatacaac tagtcttact 540
tattgatttt gcacattcat ggaatgaatc gtgggttgaa aaaatggaag aagggaactc 600
gagatgttgg tatgcagcct tgttatcagc tacagctctg aattatctgc tgtctttagt 660
tgctatcgtc ctgttctttg tctactacac tcatccagcc agttgttcag aaaacaaggc 720
gttcatcagt gtcaacatgc tcctctgcgt tggtgcttct gtaatgtcta tactgccaaa 780
aatccaagaa tcacaaccaa gatctggttt gttacagtct tcagtaatta cagtctacac 840
aatgtatttg acatggtcag ctatgaccaa tgaaccagaa acaaattgca acccaagtct 900
actaagcata attggctaca atacaacaag cactgtccca aaggaagggc agtcagtcca 960
gtggtggcat gctcaaggaa ttataggact aattctcttt ttgttgtgtg tattttattc 1020
cagcatccgt acttcaaaca atagtcaggt taataaactg actctaacaa gtgatgaatc 1080
tacattaata gaagatggtg gagctagaag tgatggatca ctggaggatg gggacgatgt 1140
tcaccgaget gtagataatg aaagggatgg tgtcacttac agttatteet tetttcactt 1200
catgetttte etggetteae tttatateat gatgaceett accaactggt acaggtatga 1260
accetetegt gagatgaaaa gteagtggae agetgtetgg gtgaaaatet etteeagttg 1320
gattggcatc gtgctgtatg tttggacact cgtggcacca cttgttctta caaatcgtga 1380
ttttgactga gtgagacttc tagcatgaaa gtcccacttt gattattgct tatttgaaaa 1440
cagtattccc aacttttgta aagttgtgta tgtttttgct tcccatgtaa cttctccagt 1500
gttctggcat gaattagatt ttactgcttg tcattttgtt attttcttac caagtgcatt 1560
gatatgtgaa gtagaatgaa ttgcagagga aagttttatg aatatggtga tgagttagta 1620
aaagtggcca ctattgggct tattctctgc tctatagttg tgaaatgaag agtgaaaaca 1680
aatttgtttg actattttaa aattatatta gaccttaagc tgttttagca agcattaaag 1740
caaatgtatg gctgcctttt gaaatatttg atgtgttgcc tggcaggata ctgcaaagaa 1800
catggtttat tttaaaattt ataaacaagt cacttaaatg ccagttgtct gaaaaatctt 1860
ataaggtttt accettgata eggaatttac acaggtaggg agtgtttagt ggacaatagt 1920
gtaggttatg gatggaggtg tcggtactaa attgaataac gagtaaataa tcttacttgg 1980
gtagagatgg cctttgccaa caaagtgaac tgttttggtt gttttaaact catgaagtat 2040
gggttcagtg gaaatgtttg gaactctgaa ggatttagac aaggttttga aaaggataat 2100
catgggttag aaggaagtgt ttgaaagtca ctttgaaagt tagttttggg ccagcacggt 2160
agctcaccct tgtaatccca gcactttggg aggctgaggt gggtagatta cttgagccca 2220
ggaattcaag accagcctgg gcaacatggt gaaaccctgt ttctataaaa aataatctgg 2280
getttgtage atatgeetgt ggteeeaget actgaggagg etgaggtggg aggattgett 2340
gageceagga ggeagaggtt geagtgagee aaggteaegt eactgeaete tageetggge 2400
aacagagtaa gacaaaaaa tatatatata ttgaaatcaa aggaggcaaa attttgacag 2460
ggaaggaagt aactgcaaaa cactaggctt tagtaggtac ttatataaaa tctagtccag 2520
ttctctcatt taaaaaaatg aagacactga agtacagact taaatagctc agatagctaa 2580
ttaggaaatt tcaagttggc caataatagc attctctctg acatttaaaa ataatttcta 2640
ttcaaaatac atgcataatt gattttacac ctcattactg gtggataatt tatgtgatgt 2700
ggattgctgg tgtccagcat gacccataaa caggtcagaa gaatgatgga atgttttaga 2760
ataaacteet gettatagta taetacacag tteaaaagat gtttaaaaatg ettttgtatt 2820
tactgccatg taattgaaat atatagatta ttgtaacctt tcaacctgaa aatcaagcag 2880
tatgagagtt tagttatttg tatgtgtcac tagtgtctaa tgaagctttt aaaatctaca 2940
atttcttctt taaaaatatt tattaatgtg aatggaatat aacaattcag cttaattccc 3000
```

caaccttatt ctgtgtgtag acattgtatt ccacaatttt gaatggctgt gttttacctc 3060 taaataaatg aattcagaga aaaaaaaaaa aaaaaaaaa aaa 3103

<210> 70

<211> 453

<212> PRT

<213> Homo sapiens

<400> 70

Met Gly Ser Val Leu Gly Leu Cys Ser Met Ala Ser Trp Ile Pro Cys

1 10 15

Leu Cys Gly Ser Ala Pro Cys Leu Leu Cys Arg Cys Cys Pro Ser Gly
20 25 30

Asn Asn Ser Thr Val Thr Arg Leu Ile Tyr Ala Leu Phe Leu Leu Val 35 45

Gly Val Cys Val Ala Cys Val Met Leu Ile Pro Gly Met Glu Glu Gln 50 60

Leu Asn Lys Ile Pro Gly Phe Cys Glu Asn Glu Lys Gly Val Val Pro 65 70 75 80

Cys Asn Ile Leu Val Gly Tyr Lys Ala Val Tyr Arg Leu Cys Phe Gly
85 90 95

Leu Ala Met Phe Tyr Leu Leu Leu Ser Leu Leu Met Ile Lys Val Lys
100 105 110

Ser Ser Ser Asp Pro Arg Ala Ala Val His Asn Gly Phe Trp Phe Phe 115 120 125

Lys Phe Ala Ala Ala Ile Ala Ile Ile Ile Gly Ala Phe Phe Ile Pro 130 140

Glu Gly Thr Phe Thr Thr Val Trp Phe Tyr Val Gly Met Ala Gly Ala 145 150 155 160

Phe Cys Phe Ile Leu Ile Gln Leu Val Leu Leu Ile Asp Phe Ala His 165 170 175

Ser Trp Asn Glu Ser Trp Val Glu Lys Met Glu Glu Gly Asn Ser Arg 180 185 190

Cys Trp Tyr Ala Ala Leu Leu Ser Ala Thr Ala Leu Asn Tyr Leu Leu 195 200 205

Ser Leu Val Ala Ile Val Leu Phe Phe Val Tyr Tyr Thr His Pro Ala 210 215 220

Ser Cys Ser Glu Asn Lys Ala Phe Ile Ser Val Asn Met Leu Leu Cys 225 230 235 240

Val Gly Ala Ser Val Met Ser Ile Leu Pro Lys Ile Gln Glu Ser Gln 245 250 255

Pro Arg Ser Gly Leu Leu Gln Ser Ser Val Ile Thr Val Tyr Thr Met 260 265 270

Tyr Leu Thr Trp Ser Ala Met Thr Asn Glu Pro Glu Thr Asn Cys Asn Pro Ser Leu Leu Ser Ile Ile Gly Tyr Asn Thr Thr Ser Thr Val Pro 295 Lys Glu Gly Gln Ser Val Gln Trp Trp His Ala Gln Gly Ile Ile Gly Leu Ile Leu Phe Leu Cys Val Phe Tyr Ser Ser Ile Arg Thr Ser 330 Asn Asn Ser Gln Val Asn Lys Leu Thr Leu Thr Ser Asp Glu Ser Thr 340 345 Leu Ile Glu Asp Gly Gly Ala Arg Ser Asp Gly Ser Leu Glu Asp Gly 360 Asp Asp Val His Arg Ala Val Asp Asn Glu Arg Asp Gly Val Thr Tyr 375 Ser Tyr Ser Phe Phe His Phe Met Leu Phe Leu Ala Ser Leu Tyr Ile 385 390 Met Met Thr Leu Thr Asn Trp Tyr Arg Tyr Glu Pro Ser Arg Glu Met 405 Lys Ser Gln Trp Thr Ala Val Trp Val Lys Ile Ser Ser Ser Trp Ile Gly Ile Val Leu Tyr Val Trp Thr Leu Val Ala Pro Leu Val Leu Thr 435 440 Asn Arg Asp Phe Asp 450 <210> 71 <211> 1981 <212> DNA <213> Homo sapiens <400> 71 gagatccaag ttgggagcag ctctgcgtgc ggggcctcag agaatgaggc cggcgttcgc 60 cgaccgtgct ggctgctcgg cctcgggggc ctgctacagc ctgcaccacg ctaccatgaa 180 geggeaggeg geegaggagg cetgeateet gegaggtggg gegeteagea ceqtqeqtqc 240 gggegeegag etgegegetg tgetegeget eetgegggea ggeeeaggge eeggaggggg 300 ctccaaagac ctgctgttct gggtcgcact ggagcgcagg cgttcccact gcaccctgga 360 gaacgageet ttgeggggtt teteetgget gteeteegae eeeggeggte tegaaagega 420 cacgctgcag tgggtggagg agccccaacg ctcctgcacc gcgcggagat gcgcggtact 480 ccaggccacc ggtggggtcg agcccgcagg ctggaaggag atgcgatgcc acctgcgcgc 540 caacggctac ctgtgcaagt accagtttga ggtcttgtgt cctgcgccgc gccccggggc 600 egectetaae ttgagetate gegegeeett eeagetgeae agegeegete tggaetteag 660 tecacetggg accgaggtga gtgcgctctg ceggggacag etcecgatet cagttacttg 720 categeggae gaaateggeg etegetggga caaacteteg ggegatgtgt tgtgteeetg 780 ccccgggagg tacctccgtg ctggcaaatg cgcagagctc cctaactgcc tagacgactt 840 gggaggettt geetgegaat gtgetaeggg ettegagetg gggaaggaeg geegetettg 900 tgtgaccagt ggggaaggac agccgaccct tggggggacc ggggtgccca ccaggcgccc 960 gccggccact gcaaccagcc ccgtgccgca gagaacatgg ccaatcaggg tcgacgagaa 1020

```
gctgggagag acaccacttg tccctgaaca agacaattca gtaacatcta ttcctgagat 1080
 teetegatgg ggateacaga geacgatgte taccetteaa atgteeette aageegagte 1140
 aaaggccact atcaccccat cagggagcgt gatttccaag tttaattcta cgacttcctc 1200
 tgccactcet caggetttcg actectcete tgccgtggte ttcatatttg tgagcacage 1260
 agtagtagtg ttggtgatct tgaccatgac agtactgggg cttgtcaagc tctgcttca 1320
 cgaaagcccc tcttcccagc caaggaagga gtctatgggc ccgccgggcc tggagagtga 1380
 tectgagece getgetttgg getecagtte tgcacattge acaaacaatg gggtgaaagt 1440
 cggggactgt gatctgcggg acagagcaga gggtgccttg ctggcggagt cccctcttgg 1500
 ctctagtgat gcatagggaa acaggggaca tgggcactcc tgtgaacagt ttttcacttt 1560
 tgatgaaacg gggaaccaag aggaacttac ttgtgtaact gacaatttct gcagaaatcc 1620
 cccttcctct aaattccctt tactccactg aggagctaaa tcagaactgc acactccttc 1680
 cctgatgata gaggaagtgg aagtgccttt aggatggtga tactggggga ccgggtagtg 1740
 ctggggagag atattttctt atgtttattc ggagaatttg gagaagtgat tgaacttttc 1800
 aagacattgg aaacaaatag aacacaatat aatttacatt aaaaaataat ttctaccaaa 1860
 atggaaagga aatgttctat gttgttcagg ctaggagtat attggttcga aatcccaggg 1920
<210> 72
<211> 490
<212> PRT
<213> Homo sapiens
<400> 72
Met Arg Pro Ala Phe Ala Leu Cys Leu Leu Trp Gln Ala Leu Trp Pro
Gly Pro Gly Gly Glu His Pro Thr Ala Asp Arg Ala Gly Cys Ser
Ala Ser Gly Ala Cys Tyr Ser Leu His His Ala Thr Met Lys Arg Gln
                            40
Ala Ala Glu Glu Ala Cys Ile Leu Arg Gly Gly Ala Leu Ser Thr Val
Arg Ala Gly Ala Glu Leu Arg Ala Val Leu Ala Leu Leu Arg Ala Gly
Pro Gly Pro Gly Gly Ser Lys Asp Leu Leu Phe Trp Val Ala Leu
Glu Arg Arg Ser His Cys Thr Leu Glu Asn Glu Pro Leu Arg Gly
                               105
Phe Ser Trp Leu Ser Ser Asp Pro Gly Gly Leu Glu Ser Asp Thr Leu
                           120
Gln Trp Val Glu Glu Pro Gln Arg Ser Cys Thr Ala Arg Arg Cys Ala
                       135
Val Leu Gln Ala Thr Gly Gly Val Glu Pro Ala Gly Trp Lys Glu Met
                   150
Arg Cys His Leu Arg Ala Asn Gly Tyr Leu Cys Lys Tyr Gln Phe Glu
               165 .
                                  170
Val Leu Cys Pro Ala Pro Arg Pro Gly Ala Ala Ser Asn Leu Ser Tyr
                              185
```

Arg Ala Pro Phe Gln Leu His Ser Ala Ala Leu Asp Phe Ser Pro Pro 195 200 205

- Gly Thr Glu Val Ser Ala Leu Cys Arg Gly Gln Leu Pro Ile Ser Val 210 215 220
- Thr Cys Ile Ala Asp Glu Ile Gly Ala Arg Trp Asp Lys Leu Ser Gly 225 235 240
- Asp Val Leu Cys Pro Cys Pro Gly Arg Tyr Leu Arg Ala Gly Lys Cys 245 250 255
- Ala Glu Leu Pro Asn Cys Leu Asp Asp Leu Gly Gly Phe Ala Cys Glu 260 265 270
- Cys Ala Thr Gly Phe Glu Leu Gly Lys Asp Gly Arg Ser Cys Val Thr 275 280 285
- Ser Gly Glu Gly Gln Pro Thr Leu Gly Gly Thr Gly Val Pro Thr Arg
  290 295 300
- Arg Pro Pro Ala Thr Ala Thr Ser Pro Val Pro Gln Arg Thr Trp Pro 305 310 315 320
- Ile Arg Val Asp Glu Lys Leu Gly Glu Thr Pro Leu Val Pro Glu Gln
  325 330 335
- Asp Asn Ser Val Thr Ser Ile Pro Glu Ile Pro Arg Trp Gly Ser Gln
  340 345 350
- Ser Thr Met Ser Thr Leu Gln Met Ser Leu Gln Ala Glu Ser Lys Ala 355 360 365
- Thr Ile Thr Pro Ser Gly Ser Val Ile Ser Lys Phe Asn Ser Thr Thr 370 375 380
- Ser Ser Ala Thr Pro Gln Ala Phe Asp Ser Ser Ser Ala Val Val Phe 385 390 395 400
- Ile Phe Val Ser Thr Ala Val Val Val Leu Val Ile Leu Thr Met Thr 405 410 415
- Val Leu Gly Leu Val Lys Leu Cys Phe His Glu Ser Pro Ser Ser Gln
  420 425 430
- Pro Arg Lys Glu Ser Met Gly Pro Pro Gly Leu Glu Ser Asp Pro Glu 435 440 445
- Pro Ala Ala Leu Gly Ser Ser Ser Ala His Cys Thr Asn Asn Gly Val 450 460
- Lys Val Gly Asp Cys Asp Leu Arg Asp Arg Ala Glu Gly Ala Leu Leu 465 470 480
- Ala Glu Ser Pro Leu Gly Ser Ser Asp Ala 485 490

<210> 73 <211> 3098

```
<212> DNA
 <213> Homo sapiens
 <400> 73
 aggaaagcca gaacaagttc ttcaagctgc ccgtgtccgt ggtcaacacc acactgccgt 60
 gegtggeeta egtgetgetg teactegtgt acttgeeegg egtgetggeg getgeeetge 120
 agetgeggeg eggeaceaag taccageget teecegactg getggaceae tggetacage 180
 accgcaagca gatcgggctg ctcagcttct tctgcgccgc cctgcacgcc ctctacagct 240
 tetgettgee getgegeege geceaeeget acgaeetggt caacetggea gteaageagg 300
 tettggccaa caagagccae etetgggtgg aggaggaggt etggeggatg gagatetace 360
 tetecetggg agtgetggee eteggeaegt tgtecetget ggeegtgaee teaetgeegt 420
 ccattgcaaa ctcgctcaac tggagggagt tcagcttcgt tcagtcctca ctgggctttg 480
 tggccctcgt gctgagcaca ctgcacacgc tcacctacgg ctggacccgc gccttcgagg 540
 agageegeta caagttetae etgeeteeca eetteaeget caegetgetg gtgeeetgeg 600
 tegteateet ggecaaagee etgtttetee tgeeetgeat cageegeaga etegeeagga 660
 teeggagagg etgggagagg gagageacea teaagtteae getgeecaea gaecaegeee 720
 tggccgagaa gacgagccac gtatgaggtg cctgccctgg gctctggacc ccgggcacac 780
gagggacggt gccctgagcc cgttaggttt tctttcttg gtggtgcaaa gtggtataac 840
tgtgtgcaaa taggaggttt gaggtccaaa ttcctgggac tcaaatgtat gcagtactat 900
tcagaatgat atacacacat atgtgtatat gtatttacat atattccaca tatataacag 960
gatttgcaat tatacatagc tagctaaaaa gttgggtctc tgagatttca acttgtagat 1020
ttaaaaacaa gtgccgtacg ttaagagaag agcagatcat gctattgtga catttgcaga 1080
gatatacaca cactttttgt acagaagagg cttgtgctgt ggtgggttcg atttatccct 1140
geecacecca teeceacaac tteeettttg ctaetteece aaggetettg cagagetagg 1200
gctctgaagg ggagggaagg caacggctct gcccagagcc atccctggag catgtgagca 1260
geggetggte tettecetee acetggggca geagcaggag geetggggag gaggaaaate 1320
aggeagtegg cetggagtet gtgeetggte etttgeeegg tggtgggagg atggagggat 1380
tgggctgaag ctgctccacc tcatccttgc tgagtggggg agacattttc cctgaaagtc 1440
agaagtcacc atagagcctg caaatggatc ctcctgtgag agtgacgtca cctcctttcc 1500
agagecatta gtgageetgg ettgggaaca agtgtaattt eetteeetee tttaacetgg 1560
cgatgagcgt cctttaaacc actgtgcctt ctcacccttt ccatcttcag tttgaacgac 1620
tcccaggaag gcctagagca gaccctttag aaatcagccc aagggggaga gcaagagaaa 1680
acactetagg gagtaaaget eeeegggegt cagagttgag eeetgeetgg getgaaggae 1740
tgtcttcacg aagtcagtcc tgaggaaaaa tattggggac tccaaatgtc ctctggcaga 1800
ggacccagaa aaccacactg gctccaactt cctcctcatg gggcattaca cttcaaaaca 1860
gtggggagca acttttccac caaagctaca aacctaaaat gctgctgccc caaagcacaa 1920
gagggaagag caccgccggg gccacaggac gtctgtcctc cagtcacagg ccatccttgc 1980
tgctccctac tgactctagc ttacttcccc tgtgaagaaa caggtgttct cggctgagcc 2040
cccaaccete tgcagaacca ggttgatetg ccacagaaaa agcatetttg aagacaaaga 2100
gggtgaggte tteatgagte teetgggeee aaageeatet tetgatggaa ggaagagagt 2160
agggccagtg aaggctgccc agagagaatg tcacagatga ggctgcccct gccccctccc 2220
cgccagggag gtttcatgag ctcatgtcta tgcagcacat aagggttctt cagtgaaaag 2280
caggagaaga gcccactgca aggatagctc attaggcaca tgaccgatgc agggaaggcc 2340
atgeegggga agetetteet geaggtattt tecatetget gtgeeaagge tgageggeag 2400
aaacttgtct cataaattgg cactgatgga gcatcagctg tggcccacag agagccttgc 2460
tgagaagggg gcaggtaaag cagagatttt agcattgcct tggcataaca agggcccatc 2520
gattecetae taatgagagg cagggagage atgggeaatg gagacecace aatgateeee 2580
aaccccggtg ggtactggct gcctgccctg ggccagggaa tggctcctta taccaaagat 2640
getggeacat ageagaacee agtgeaegte eteceettee cacceacete tggetgaagg 2700
tgctcaagag ggaagcaatt ataaggtggg tggcaggagg gaacaggtgc cacctgctgg 2760
acaatcacac gaaaggcagg cgggctgtgt actgggccct gactgtgcgt ccactgctgt 2820
cttccctacc tcaccagget actggcagca gcatcccgag agcacatcat ctccacagcc 2880
tggtaaattc catgtgcctc tgggtacaaa agtgcctcaa cgacatgctc tggaaatccc 2940
aaatgccaca gtctgaggtt gatatctaaa atctatgcct tcaaaagagt ctctgttttt 3000
ttttttttaa cctggtagac ggtataaaag cagtgcaaat aaacacctaa ccttctgcaa 3060
aaaaaaaaa aaaaaaaaa aaaaaaaaa
```

<210> 74

<211> 132

<212> PRT

<213> Homo sapiens <400> 74 Met Glu Ile Tyr Leu Ser Leu Gly Val Leu Ala Leu Gly Thr Leu Ser Leu Leu Ala Val Thr Ser Leu Pro Ser Ile Ala Asn Ser Leu Asn Trp 25 Arg Glu Phe Ser Phe Val Gln Ser Ser Leu Gly Phe Val Ala Leu Val 40 Leu Ser Thr Leu His Thr Leu Thr Tyr Gly Trp Thr Arg Ala Phe Glu Glu Ser Arg Tyr Lys Phe Tyr Leu Pro Pro Thr Phe Thr Leu Thr Leu Leu Val Pro Cys Val Val Ile Leu Ala Lys Ala Leu Phe Leu Leu Pro Cys Ile Ser Arg Arg Leu Ala Arg Ile Arg Arg Gly Trp Glu Arg Glu 105 Ser Thr Ile Lys Phe Thr Leu Pro Thr Asp His Ala Leu Ala Glu Lys Thr Ser His Val 130 <210> 75 <211> 922 <212> DNA <213> Homo sapiens <400> 75 gtgaaatgag aaaggcccag aacgtgcagg tctgcggagg ggaagtgtcc tgagtgaagg 60 aggggacccc catcctgggg gatgctggga gtgagtgagt gagtgagatg gctgagtgag 120 ggttatgggg agcctgaggt tttatgggcc tgtgtatccc cttctcccgg ccccagcctg 180 cetecetect geeegeetgg eccaeaggte teeetetggt ecctgteeet etggtggttg 240 gggatggagc ggcagcaagg ggtgtaatgg ggctgggttc tgtcttctac aggccacccc 300 gaggtcctca gtggttgcct ggggagccgg acggggctcc tgaggggtac aggttgggtg 360 ggccctccct gagggtctgg ggtcaggctt tggcctctgc tgcctctcag tcaccaagtc 420 acctecetet gaaaateeag teeettettt ggatgteett gtgagteact etgggeetgg 480 ctgtcgtccc tcctcagctt cttgttcctg ggacaagggt caagccagga tgggcccagg 540 cctgggatcc cccacccag gaccccagg cccctcccc tgctgctttg cggggggcag 600 ggcagaaatg gactcctttt gggtccccga ggtggggtcc cctcccagcc ctgcatcctc 660 cgtgccgtag acctgctccc cagaggaggg gccttgaccc acaggacgtg tggtggcgcc 720 tggcactcag ggaccccag ctgccccagc cctggtctct ggcgcatctc ttccctcttg 780 tcccgaagat ctgcgcctct agtgcctttt gaggggttcc catcatccct ccctgatatt 840 gtattgaaaa tattatgcac actgttcatg cttctactaa tcaataaacg ctttatttaa 900 aaaaaaaaa aa 922

<210> 76

<211> 106

<212> PRT

<213> Homo sapiens

<400> 76

```
Met Gly Leu Cys Ile Pro Phe Ser Arg Pro Gln Pro Ala Ser Leu Leu
                                   1.0
Pro Ala Trp Pro Thr Gly Leu Pro Leu Val Pro Val Pro Leu Val Val
Gly Asp Gly Ala Ala Arg Gly Val Met Gly Leu Gly Ser Val Phe
                             40
Tyr Arg Pro Pro Arg Gly Pro Gln Trp Leu Pro Gly Glu Pro Asp Gly
Ala Pro Glu Gly Tyr Arg Leu Gly Gly Pro Ser Leu Arg Val Trp Gly
                     70
Gln Ala Leu Ala Ser Ala Ala Ser Gln Ser Pro Ser His Leu Pro Leu
Lys Ile Gln Ser Leu Leu Trp Met Ser Leu
            100
<210> 77
<211> 823
<212> DNA
<213> Homo sapiens
<400> 77
ageceettge ageaceeget ggetacetea ecetggtgee eetgetggee aceatgetet 60
tcatcatggg ctacgccgtg ggctggggtc ccatcacctg gctgctcatg tctgaggtcc 120
tgcccctgcg tgcccgtggc gtggcctcag ggctctgcgt gctggccagc tggctcaccg 180
cettegteet caccaagtee tteetgeeag tggtgageae etteggeete caggtgeett 240
tettettett egeggeeate tgettggtga geetggtgtt cacaggetge tgtgtgeeeg 300
agaccaaggg acggtccctg gagcagatcg agtccttctt ccgcacgggg agaaggtcct 360
tettgegeta ggtcaaggte ceegeetgga gggggecaaa ceeccagtgg etgggeetet 420
gtgttggctg tgcaaggaag acceggettt geeetcacaa gtettatggg caccacaggg 480
aacatcctgg acttaaaaag ccagggcagg ccgggcacag tggctcacgc ctgtaatccc 540
agcactttgg gaggccaaag caggtggatt acccaaggcc aggagttcaa gaccagcctg 600
gccaacatgg tgaaaccccg tctctactaa aaaatacaaa aaagctgggt gtggtggcac 660
acaccegtag ttecagetae ttgggagget gaggeageat tgettgaace egggaggtgg 720
aggetgeaat gagetgagat catgecattg cactecagee tgggeaacga gagtgaaact 780
<210> 78
<211> 105
<212> PRT
<213> Homo sapiens
Met Leu Phe Ile Met Gly Tyr Ala Val Gly Trp Gly Pro Ile Thr Trp
Leu Leu Met Ser Glu Val Leu Pro Leu Arg Ala Arg Gly Val Ala Ser
Gly Leu Cys Val Leu Ala Ser Trp Leu Thr Ala Phe Val Leu Thr Lys
Ser Phe Leu Pro Val Val Ser Thr Phe Gly Leu Gln Val Pro Phe Phe
    50
```

```
Phe Phe Ala Ala Ile Cys Leu Val Ser Leu Val Phe Thr Gly Cys Cys
Val Pro Glu Thr Lys Gly Arg Ser Leu Glu Gln Ile Glu Ser Phe Phe
                 85
Arg Thr Gly Arg Arg Ser Phe Leu Arg
            100
<210> 79
<211> 1224
<212> DNA
<213> Homo sapiens
<400> 79
aatgaactgg gagctgctgc tgtggctgct ggtgctgtgc gcgctgctcc tgctcttggt 60
gcagctgctg cgcttcctga gggctgacgg cgacctgacg ctactatggg ccgagtggca 120
gggacgacgc ccagaatggg agctgactga tatggtggtg tgggtgactg gagcctcgag 180
tggaattggt gaggagctgg cttaccagtt gtctaaacta ggagtttctc ttgtgctgtc 240
agccagaaga gtgcatgagc tggaaagggt gaaaagaaga tgcctagaga atggcaattt 300
ggctaccaaa gctgttctcc aggagtttgg tagaatcgac attctggtca acaatggtgg 420
aatgteecag egttetetgt geatggatae eagettggat gtetacagaa agetaataga 480
gcttaactac ttagggacgg tgtccttgac aaaatgtgtt ctgcctcaca tgatcgagag 540
gaagcaagga aagattgtta ctgtgaatag catcctgggt atcatatctg tacctctttc 600
cattggatac tgtgctagca agcatgctct ccggggtttt tttaatggcc ttcgaacaga 660
acttgccaca tacccaggta taatagtttc taacatttgc ccaggacctg tgcaatcaaa 720
tattgtggag aattccctag ctggagaagt cacaaagact ataggcaata atggagacca 780
gtcccacaag atgacaacca gtcgttgtgt gcggctgatg ttaatcagca tggccaatga 840
tttgaaagaa gtttggatct cagaacaacc tttcttgtta gtaacatatt tgtggcaata 900
catgccaacc tgggcctggt ggataaccaa caagatgggg aagaaaagga ttgagaactt 960
taagagtggt gtggatgcag actcttctta ttttaaaatc tttaagacaa aacatgactg 1020
aaaagagcac ctgtactttt caagccactg gagggagaaa tggaaaacat gaaaacagca 1080
atcttcttat gcttctgaat aatcaaagac taatttgtga ttttactttt taatagatat 1140
gactttgctt ccaacatgga atgaaataaa aaataaataa taaaagattg ccatgaatct 1200
tgcaaaaaa aaaaaaaaa aaaa
                                                                1224
<210> 80
<211> 339
<212> PRT
<213> Homo sapiens
Met Asn Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu
                 5
Leu Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu
Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu
Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu
    50
Glu Leu Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser
                    70
                                       75
```

Ala Arg Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu 85 90 95

- Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu 100 105 110
- Thr Asp Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu 115 120 125
- Phe Gly Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg 130 135 140
- Ser Leu Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu 145 150 155 160
- Leu Asn Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His 165 170 175
- Met Ile Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu 180 185 190
- Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His 195 200 205
- Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr 210 215 220
- Pro Gly Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn 225 230 235 240
- Ile Val Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn 245 250 255
- Met Leu Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu 275 280 285
- Gln Pro Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp 290 295 300
- Ala Trp Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe 305 310 315 320
- Lys Ser Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr 325 330 335

Lys His Asp

- <210> 81
- <211> 21
- <212> DNA
- <213> Artificial Sequence
- <220>
- <223> oligonucleotide

<210>		
	87	
<211>		
<212>		
	Artificial Sequence	
<220>		
	oligonucleotide	
<400>	87	
	ccagt agcatcagg	19
<b>55044</b>		13
<210>	88	
<211>		
<212>	<del></del>	
	Artificial Sequence	
~213/	Artificial Sequence	
<220>		
<443>	oligonucleotide	
-400-	0.0	
<400>		
tgaac	tcgga gtgctctgg	19
0.1.0		
<210>		
<211>		
<212>		
<213>	Artificial Sequence	
	·	
<220>		
<223>	oligonucleotide	
<400>		
	89 ttcag tacceteg	18
ctggc	ttcag taccetcg	18
<210>	90	18
<210><211>	90 20	18
<210><211><212>	ttcag taccctcg 90 20 DNA	18
<210><211><212>	90 20	18
<pre><tggc <210=""> &lt;211&gt; &lt;212&gt; &lt;213&gt;</tggc></pre>	ttcag taccctcg 90 20 DNA	18
<pre>&lt;210&gt; &lt;211&gt; &lt;212&gt; &lt;213&gt; &lt;220&gt;</pre>	90 20 DNA Artificial Sequence	18
<pre>&lt;210&gt; &lt;211&gt; &lt;212&gt; &lt;213&gt; &lt;220&gt;</pre>	ttcag taccctcg 90 20 DNA	18
<pre>&lt;210&gt; &lt;211&gt; &lt;212&gt; &lt;213&gt; &lt;220&gt;</pre>	90 20 DNA Artificial Sequence	18
<pre>&lt;210&gt; &lt;211&gt; &lt;212&gt; &lt;213&gt; &lt;220&gt;</pre>	90 20 DNA Artificial Sequence oligonucleotide	18
<pre>&lt;210&gt; &lt;211&gt; &lt;211&gt; &lt;212&gt; &lt;213&gt; &lt;223&gt; &lt;400&gt;</pre>	90 20 DNA Artificial Sequence oligonucleotide	18
<pre>ctggc &lt;210&gt; &lt;211&gt; &lt;212&gt; &lt;213&gt; &lt;220&gt; &lt;223&gt; &lt;400&gt; acgccc</pre>	90 20 DNA Artificial Sequence  oligonucleotide 90 etggt ggaggacctc	
<pre>&lt;210&gt; &lt;211&gt; &lt;211&gt; &lt;212&gt; &lt;213&gt; &lt;223&gt; &lt;400&gt;</pre>	90 20 DNA Artificial Sequence  oligonucleotide  90 etggt ggaggacctc	
<pre>ctggc &lt;210&gt; &lt;211&gt; &lt;212&gt; &lt;213&gt; &lt;220&gt; &lt;223&gt; &lt;400&gt; acgccc</pre>	90 20 DNA Artificial Sequence  oligonucleotide 90 etggt ggaggacctc	
ctggc <210> <211> <212> <213> <220> <223> <400> acgccc <210> <211> <212>	90 20 DNA Artificial Sequence  oligonucleotide 90 ctggt ggaggacctc 91 20 DNA	
ctggc <210> <211> <212> <213> <220> <223> <400> acgccc <210> <211> <212>	90 20 DNA Artificial Sequence  oligonucleotide  90 etggt ggaggacctc  91 20	
ctggc <210> <211> <212> <213> <220> <223> <400> acgccc <210> <211> <212>	90 20 DNA Artificial Sequence  oligonucleotide 90 ctggt ggaggacctc 91 20 DNA	
ctggc <210> <211> <212> <213> <220> <223> <400> acgccc <210> <211> <212> <213>	90 20 DNA Artificial Sequence  oligonucleotide  90 etggt ggaggacete  91 20 DNA Artificial Sequence	
ctggc <210> <211> <212> <213> <220> <223> <400> acgccc <210> <211> <212> <213>	90 20 DNA Artificial Sequence  oligonucleotide 90 ctggt ggaggacctc 91 20 DNA	
ctggc <210> <211> <212> <213> <220> <223> <400> acgccc <210> <211> <212> <213>	90 20 DNA Artificial Sequence  oligonucleotide  90 etggt ggaggacete  91 20 DNA Artificial Sequence	
ctggc <210> <211> <212> <213> <220> <223> <400> acgccc <210> <211> <212> <213>	90 20 DNA Artificial Sequence  oligonucleotide  90 etggt ggaggacete  91 20 DNA Artificial Sequence  oligonucleotide  oligonucleotide	
ctggc <210> <211> <212> <213> <220> <223> <400> acgccc <211> <212> <213> <220> <400> <210> <211> <212> <213> <400>	90 20 DNA Artificial Sequence  oligonucleotide  90 etggt ggaggacete  91 20 DNA Artificial Sequence  oligonucleotide  oligonucleotide	
ctggc <210> <211> <212> <213> <220> <223> <400> acgccc <211> <212> <213> <220> <400> <210> <211> <212> <213> <400>	90 20 DNA Artificial Sequence  oligonucleotide  90 etggt ggaggacete  91 20 DNA Artificial Sequence  oligonucleotide  91 20 DNA Artificial Sequence	20
ctggc <210> <211> <212> <213> <220> <223> <400> acgccc <211> <212> <213> <220> <400> <210> <211> <212> <213> <400>	90 20 DNA Artificial Sequence  oligonucleotide  90 ctggt ggaggacctc  91 20 DNA Artificial Sequence  oligonucleotide  91 20 ctggt ggaggacctc  91 20 DNA Artificial Sequence	20
ctggc <210> <211> <212> <213> <220> <223> <400> acgccc <211> <212> <213> <400> and acgccc <210 <212> <213> <400> and acgccc <210 <212 <213> <220> <220> <223>	90 20 DNA Artificial Sequence  oligonucleotide 90 ctggt ggaggacctc 91 20 DNA Artificial Sequence  oligonucleotide 91 2tcaa ctattggggc	20
ctggc <210> <211> <212> <213> <220> <223> <400> acgccc <211> <212> <213> <400> <211> <212> <213> <220> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210> <210>	90 20 DNA Artificial Sequence  oligonucleotide  90 etggt ggaggacete  91 20 DNA Artificial Sequence  oligonucleotide  91 21  ctcaa ctattggggc	20

<220>	oligonucleotide	
<400>		
	aattg totgtagaaa g	21
<210>		
<211>		
<212>		
<213>	Artificial Sequence	
<220>		
<223>	oligonucleotide	
<400>	93	
ctacto	ctgga gtcagccgc	19
<210>		
<211>		
<212>		
<213>	Artificial Sequence	
<220>		
<223>	oligonucleotide	
<400>		
aacatt	gtgg aaacagtgac c	21
<210>		
<211>		
<212>		
<213>	Artificial Sequence	
<220>		
<223>	oligonucleotide	
<400>	95	
ggttgg	agag teageacteg	20
<210>	96	
<211>		
<212>		
<213>	Artificial Sequence	
<220>		
	oligonucleotide	
12232	oligonacieotide	
<400>		
tgtgag	agca cagactgcg	19
<210>	97	
<211>	20	
<212>		
<213>	Artificial Sequence	
<220>	•	
	oligonucleotide	
<400>	97	

## PCT/US99/19351 WO 00/11015 ctgagttgat tagaatgctg 20 <210> 98 <211> 19 <212> DNA <213> Artificial Sequence <220> <223> oligonucleotide <400> 98 tgtacctcaa gcacagccc 19 <210> 99 <211> 18 <212> DNA <213> Artificial Sequence <220> <223> oligonucleotide <400> 99 cacatcacaa agggcacc 18 <210> 100 <211> 19 <212> DNA <213> Artificial Sequence <220> <223> oligonucleotide <400> 100 agaccettgg acctggcag 19 <210> 101 <211> 19 <212> DNA <213> Artificial Sequence <220> <223> oligonucleotide <400> 101 gaacctggag caaggacac 19 <210> 102 <211> 19 <212> DNA <213> Artificial Sequence <220> <223> oligonucleotide <400> 102 cccgtggaag tagagagcc 19 <210> 103 <211> 21

<212> DNA

<213>	Artificial Sequence	
<220>		
<223>	oligonucleotide	
<400>	103	
ttcaa	tgggt gaattgtatg g	21
<210>	104	
<211>	20	
<212>	DNA	
<213>	Artificial Sequence	
<220>		
<223>	oligonucleotide	
<400>	104	
tggaa	tagca tgactgggtg	20
<210>	105	
<211>	21	
<212>	DNA	
<213>	Artificial Sequence	
<220>		
<223>	oligonucleotide	
<400>		
tctcag	gaagc atcaccaact g	21
<210>	106	
<211>		
<212>	DNA	
<213>	Artificial Sequence	
<220>		
<223>	oligonucleotide	
<400>	106	
attctg	getet teetetteet e	21
<210>	107	
<211>	20	
<212>		
<213>	Artificial Sequence	
<220>		
<223>	oligonucleotide	
<400>		
cctcac	ctgag ggtgaactgc	20
<210>	108	
<211>		
<212>		
<213>	Artificial Sequence	
<220>		
-223	oligonucleatido	

WO 00/11015	PCT/US99/193
<400> 108	
tctgagggaa gaagggaatg	20
<210> 109	
<211> 19	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> oligonucleotide	
<400> 109	
ttcaacagag ctgggcaag	19
<210> 110	•
<211> 18	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> oligonucleotide	
<400> 110	·
tgtcgtccgg tcactgtg	18
<210> 111	
<211> 20	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> oligonucleotide	
<400> 111	
ctcataaagc aagagctggc	20
<210> 112	
<211> 19	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> oligonucleotide	
<400> 112	
acggaagcac cagcactag	19
<210> 113	
<211> 21	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> oligonucleotide	
<400> 113	
cccaaaagca gtattcaaaa c	21
<210> 114	
<211> 18	

<212> DNA <213> Artificial Sequen	ce
-220	
<220> <223> oligonucleotide	
<400> 114	
accttgacac ctggctcc	18
<210> 115	
<211> 21	
<212> DNA	
<213> Artificial Sequen	ce
<220>	
<223> oligonucleotide	
<400> 115	
actttcctct gcaattcatt c	21
-210- 116	
<210> 116 <211> 20	
<212> DNA	
<213> Artificial Sequence	20
Deque	
<220>	
<223> oligonucleotide	
<400> 116	
teacttetee aaatteteeg	20
•	
<210> 117	
<211> 20	
<212> DNA <213> Artificial Sequence	•
all sequent	
<220>	
<223> oligonucleotide	
<400> 117	
tgggtctctg agatttcaac	20
	20
<210> 118	
<211> 19	
<212> DNA	
<213> Artificial Sequence	e
<220>	
<223> oligonucleotide	
<100> 110	
<400> 118 tcactcactc ccagcatcc	
cageatee	19
<210> 119	
<211> 18	
<212> DNA	
<213> Artificial Sequenc	e
<220>	
<223> oligonucleotide	

```
<400> 119
cagacatgag cagccagg
                                                                 18
<210> 120
<211> 19
<212> DNA
<213> Artificial Sequence
<220>
<223> oligonucleotide
<400> 120
tgcctcacat gatcgagag
                                                                 19
<210> 121
<211> 51
<212> PRT
<213> Homo sapiens
<400> 121
Met Gly Leu Lys Asn Ser Arg Phe Trp Glu Pro Ser Met Leu Ser Leu
                5
Ser Pro Leu Leu Ser Thr Ser Leu Pro Asn Glu Arg Val Thr Glu Asn
Cys Phe Phe Ile Asn Arg Ser Phe Leu Ile Val Ser Gly Phe Asp Thr
                            40
Ser Val Val
    50
<210> 122
<211> 101
<212> PRT
<213> Homo sapiens
<400> 122
Met Glu Thr Val Met Thr Leu Glu Gly Gly Gln Lys Pro Val Met Glu
                                    10
Ser Tyr Thr Leu Leu Ser Pro Pro Glu Thr Gln Asp Glu Gly Trp
                25
Thr Leu Ala Leu Ser Leu Ala Leu Thr Tyr Arg Leu Gly Pro Gly Ser
                          40
Val Leu Leu Ala Pro Arg Ser Pro Trp Arg Leu Gln Lys Pro Pro
Ala Gly Gly Leu Pro His Ser Gln Leu Pro Ala Arg Gln Trp Gly Leu
65
                   70
Leu Arg Gln Ala Gly Pro Lys Thr Val Ser Pro Leu Gly Thr Tyr Ser
Pro Pro Ser Ile Cys
```

100

```
<210> 123
<211> 90
<212> PRT
<213> Homo sapiens
Met Arg Leu Ser Thr Val Gly Thr Val His Ser Gly Pro Pro Leu Ser
Ser Gly Leu Leu Thr Gly Ala Pro Cys His Val Val Thr Met Ala His
Arg Pro Leu Leu Leu Leu Leu Leu Leu Pro Pro Glu Glu Leu Arg
Leu Cys Phe Gly Leu Leu Val Ser Gly Gln Phe Leu Val Val Leu Leu
Arg Leu Arg Gly Pro Asp Leu Phe Leu His His Arg Ile Val His Leu
Val Phe Leu Thr Leu Arg Phe Leu Ala Cys
<210> 124
<211> 325
<212> PRT
<213> Homo sapiens
<400> 124
Met Gly Gly Ala Leu Cys Asp Val Val Leu Gln Thr Glu Arg Lys Gly
Gly Ser Val Leu Ser Tyr Ile Asn Gly Val Thr Thr Ser Lys Pro Gly
Val Ser Leu Val Tyr Ser Met Pro Ser Arg Asn Leu Ser Leu Arg Leu
Glu Gly Leu Gln Glu Lys Asp Ser Gly Pro Tyr Ser Cys Ser Val Asn
Val Gln Asp Lys Gln Gly Lys Ser Arg Gly His Ser Ile Lys Thr Leu
                     70
Glu Leu Asn Val Leu Val Pro Pro Ala Pro Pro Ser Cys Arg Leu Gln
Gly Val Pro His Val Gly Ala Asn Val Thr Leu Ser Cys Gln Ser Pro
Arg Ser Lys Pro Ala Val Gln Tyr Gln Trp Asp Arg Gln Leu Pro Ser
       115
Phe Gln Thr Phe Phe Ala Pro Ala Leu Asp Val Ile Arg Gly Ser Leu
```

135

Ser Leu Thr Asn Leu Ser Ser Ser Met Ala Gly Val Tyr Val Cys Lys 155 Ala His Asn Glu Val Gly Thr Ala Gln Cys Asn Val Thr Leu Glu Val 170 Ser Thr Gly Pro Gly Ala Ala Val Val Ala Gly Ala Val Val Gly Thr 185 Leu Val Gly Leu Gly Leu Leu Ala Gly Leu Val Leu Leu Tyr His Arg 200 Arg Gly Lys Ala Leu Glu Glu Pro Ala Asn Asp Ile Lys Glu Asp Ala 215 Ile Ala Pro Arg Thr Leu Pro Trp Pro Lys Ser Ser Asp Thr Ile Ser 225 230 Lys Asn Gly Thr Leu Ser Ser Val Thr Ser Ala Arg Ala Leu Arg Pro 250 Pro His Gly Pro Pro Arg Pro Gly Ala Leu Thr Pro Thr Pro Ser Leu 260 265 Ser Ser Gln Ala Leu Pro Ser Pro Arg Leu Pro Thr Thr Asp Gly Ala 280 His Pro Gln Pro Ile Ser Pro Ile Pro Gly Gly Val Ser Ser Ser Gly Leu Ser Arg Met Gly Ala Val Pro Val Met Val Pro Ala Gln Ser Gln 310 315 Ala Gly Ser Leu Val <210> 125 <211> 127 <212> PRT <213> Homo sapiens <400> 125 Met Ile Ser Leu Pro Gly Pro Leu Val Thr Asn Leu Leu Arg Phe Leu Phe Leu Gly Leu Ser Ala Leu Ala Pro Pro Ser Arg Ala Gln Leu Gln 25 Leu His Leu Pro Ala Asn Arg Leu Gln Ala Val Glu Gly Gly Val Val Leu Pro Ala Trp Tyr Thr Leu His Gly Glu Val Ser Ser Ser Gln 55 Pro Trp Glu Val Pro Phe Val Met Trp Phe Phe Lys Gln Lys Glu Lys Glu Asp Gln Cys Cys Pro Thr Ser Met Gly Ser Gln Gln Ala Asn Leu 85

Glu Tyr Pro Trp Ser Thr Pro Cys Pro Pro Gly Thr Cys Pro Cys Gly 100 105 110

Trp Arg Val Ser Arg Arg Lys Thr Leu Ala Pro Thr Ala Ala Pro 115 120 125

<210> 126

<211> 91

<212> PRT

<213> Homo sapiens

<400> 126

Met Asn Gly Val Thr His His Val Ala Phe Cys Val Trp Phe Leu Pro  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Leu Ser Ile Met Ile Ser Ser Ser Cys Arg Ser Met His Leu Ser Phe 20 25 30

Ile Pro Ser His Gly Ala Ile Ile Phe His Cys Val Tyr Lys Thr Thr 35 40

Phe Cys Gln Ser Thr His Pro Trp Ile Thr Ser Ala Phe Leu Lys Gly 50 60

Ala Phe Thr Ser Gln Thr Gln Phe Ser Val Gly Glu Gly Val Arg Gly 65 70 75 80

Gln Tyr Arg Ser Asp Cys Lys Arg His Lys Leu 85 90

<210> 127

<211> 84

<212> PRT

<213> Homo sapiens

<400> 127

Met Leu Phe Pro Ser Ser Ser Ser Lys Pro Phe Ser Leu Leu Ser Leu 1 5 15

Thr Ile Trp Ala Arg Leu Val Gly Arg Leu Thr Asn Arg Ile Cys Pro 20 25 30

Val Pro Pro Gly Ser Val Ala Ser Ser Met Ser Leu Gln Ala Gly Arg 35 40

Cys Gly Asn Pro Val Val Leu Pro Gln Pro Met Pro Pro Gly Leu Leu 50 60

Cys Met Asn Glu Cys Ser Leu Val Pro Gly Leu Gly Arg Gly Gln Val 65 70 75 80

Asn Ser Arg Val

<210> 128

<211> 120

<212> PRT

<213> Homo sapiens

<400> 128

Met Arg Ala Thr His Cys Gln Ala Ala Arg Met Phe Val Leu Phe Ser  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Arg Glu Gly Asn Pro Thr Gly Phe Cys Gly Asn Asn Gly Asn Leu Gln 20 25 30

Met Pro Ala Trp Asp Asp Glu Ala His Ser Glu Gln Met Leu Phe Phe 35 45

Phe Leu Arg Gln Ser Leu Ala Leu Thr Pro Arg Leu Glu Cys Ser Gly 50 60

Ala Ile Ser Ala His Cys Lys Leu Cys Leu Pro Gly Ser Ser Asp Ser 65 70 75 80

Pro Thr Ser Ala Ser Arg Val Ala Gly Ile Thr Pro Pro Cys Pro Ala 85 90 95

Asn Phe Cys Val Phe Ser Arg Asp Gly Val Ser Pro Cys Trp Pro Gly 100 105 110

Trp Ser Arg Thr Pro Asp Leu Arg 115 120

<210> 129

<211> 143

<212> PRT

<213> Homo sapiens

<400> 129

Met Ala Glu Gly Glu Lys Asn Gln Asp Phe Thr Phe Lys Lys Glu Ser  $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15$ 

Pro Ser Asp Ser Ala Val Val Leu Pro Ser Thr Pro Gln Ala Ser Ala 20 25 30

Asn Pro Ser Ser Pro Tyr Thr Asn Ser Ser Arg Lys Gln Pro Met Ser 35 40 45

Ala Thr Leu Arg Glu Arg Leu Arg Lys Thr Arg Phe Ser Phe Asn Ser 50 55 60

Ser Tyr Asn Val Val Lys Arg Leu Lys Val Glu Ser Glu Glu Asn Asp 65 70 75 80

Gln Thr Phe Ser Glu Lys Pro Ala Ser Ser Thr Glu Glu Asn Cys Leu 85 90 95

Glu Phe Glu Ser Phe Lys His Ile Asp Ser Glu Phe Glu Glu Asn

Thr Asn Leu Lys Asn Thr Leu Thr Ala Ile Ser Met Ser Val Asn Leu 115 120 125

Ser His Leu Ile Leu Asp His Ala Val Leu Ser Lys Met Ser Leu

130 135 140

<210> 130

<211> 284

<212> PRT

<213> Homo sapiens

<400> 130

Met Glu Asp Leu Asp Gln Ser Pro Leu Val Ser Ser Ser Asp Ser Pro 1 5 10

Pro Arg Pro Gln Pro Ala Phe Lys Tyr Gln Phe Val Arg Glu Pro Glu 20 25 30

Asp Glu Glu Glu Glu Glu Glu Glu Glu Glu Asp Glu Asp Glu Asp 35 40

Leu Glu Glu Leu Glu Val Leu Glu Arg Lys Pro Ala Ala Gly Leu Ser 50 60

Ala Ala Pro Val Pro Thr Ala Pro Ala Ala Gly Ala Pro Leu Met Asp
65 70 75 80

Phe Gly Asn Asp Phe Val Pro Pro Ala Pro Arg Gly Pro Leu Pro Ala 85 90

Ala Pro Pro Val Ala Pro Glu Arg Gln Pro Ser Trp Asp Pro Ser Pro 100 105 110

Val Ser Ser Thr Val Pro Ala Pro Ser Pro Leu Ser Ala Ala Val 115 120 125

Ser Pro Ser Lys Leu Pro Glu Asp Asp Glu Pro Pro Ala Arg Pro Pro 130 135 140

Pro Pro Pro Pro Ala Ser Val Ser Pro Gln Ala Glu Pro Val Trp Thr 145 150 155 160

Pro Pro Ala Pro Ala Pro Ala Ala Pro Pro Ser Thr Pro Ala Ala Pro 165 170 175

Lys Arg Arg Gly Ser Ser Gly Ser Val Asp Glu Thr Leu Phe Ala Leu 180 185 190

Pro Ala Ala Ser Glu Pro Val Ile Arg Ser Ser Ala Glu Asn Met Asp 195 200 205

Leu Lys Glu Gln Pro Gly Asn Thr Ile Ser Ala Gly Gln Glu Asp Phe 210 215 220

Pro Ser Val Leu Leu Glu Thr Ala Ala Ser Leu Pro Ser Leu Ser Pro 225 230 235 240

Leu Ser Ala Ala Ser Phe Lys Glu His Glu Tyr Leu Gly Asn Leu Ser 245 250 255

Thr Val Leu Pro Thr Glu Gly Thr Leu Gln Glu Asn Val Ser Glu Ala 260 265 270 Ser Lys Glu Val Ser Glu Lys Ala Lys Leu Tyr Ser 275 280

<210> 131

<211> 175

<212> PRT

<213> Homo sapiens

<400> 131

Met Arg Pro Ala Phe Ala Leu Cys Leu Leu Trp Gln Ala Leu Trp Pro 1 5 10 15

Gly Pro Gly Gly Glu His Pro Thr Ala Asp Arg Ala Gly Cys Ser 20 25 30

Ala Ser Gly Ala Cys Tyr Ser Leu His His Ala Thr Met Lys Arg Gln 35 40

Arg Ala Gly Ala Glu Leu Arg Ala Val Leu Ala Leu Leu Arg Ala Gly 65 70 75 80

Pro Gly Pro Gly Gly Gly Ser Lys Asp Leu Leu Phe Trp Val Ala Leu 85 90 95

Glu Arg Arg Ser His Cys Thr Leu Glu Asn Glu Pro Leu Arg Gly
100 105 110

Phe Ser Trp Leu Ser Ser Asp Pro Gly Gly Leu Glu Ser Asp Thr Leu 115 120 125

Gln Trp Val Glu Glu Pro Gln Arg Ser Cys Thr Arg Ala Glu Met Arg 130 135 140

Gly Thr Pro Gly His Arg Trp Gly Arg Ala Arg Arg Leu Glu Gly Asp 145 150 155 160

Ala Met Pro Pro Ala Arg Gln Arg Leu Pro Val Gln Val Pro Val
165 170 170

<210> 132

<211> 147

<212> PRT

<213> Homo sapiens

<400> 132

Met Leu Phe Ile Met Gly Tyr Ala Val Gly Trp Gly Pro Ile Thr Trp

1 5 10

Leu Leu Met Ser Glu Val Leu Pro Leu Arg Ala Arg Gly Val Ala Ser 20 25 30

Gly Leu Cys Val Leu Ala Ser Trp Leu Thr Ala Phe Val Leu Thr Lys 35 40

Ser Phe Leu Pro Val Val Ser Thr Phe Gly Leu Gln Val Pro Phe Phe

50 55 60

Phe Phe Ala Ala Ile Cys Leu Val Ser Leu Val Phe Thr Gly Cys Cys 65 70 75 80

Val Pro Glu Thr Lys Gly Arg Ser Leu Glu Gln Ile Glu Phe Leu Leu 85 90 95

Pro His Gly Glu Lys Val Leu Leu Ala Leu Gly Gln Gly Pro Arg Leu
100 105 110

Glu Gly Ala Lys Pro Pro Val Ala Gly Pro Leu Cys Trp Leu Cys Lys 115 120 125

Glu Asp Pro Ala Leu Pro Ser Gln Val Leu Trp Ala Pro Gln Gly Thr 130  $\,$  135  $\,$  140

Ser Trp Thr

145

International application No. PCT/US99/19351

	SIFICATION OF SUBJECT MATTER C07H 21/04; C07K 14/705; C12N 15/09;, 15/63; C12	O 1/68		
US CL :	536/23.1, 24.3; 435/7.2. 69.1, 320.1; 530/350, 300	•		
	o International Patent Classification (IPC) or to both n	ational cla	ssification and IPC	
	DS SEARCHED  cumentation searched (classification system followed	hu alassi	iention gumbols)	
	536/23.1, 24.3; 435/7.269.1, 320.1; 530/350, 300 .	by Classii	icadon symbols)	
0.3. :	330/23.1, 24.3, 433/1.2.239.1, 320.1,.32W330, 300 .			
Documentati	on searched other than minimum documentation to the	extent that	such documents are included	in the fields searched
Electronic d	ata base consulted during the international search (nat	me of date	base and, where practicable,	search terms used)
PROT37,	E, JAPIO, BIOSIS, WPIDS, CAPLUS, EMBASE, 1 SPTREMBL19, EMBL58 ns: secreted proteins, 98862, 98846, VB11	N-GENES	EQ35, N-ISSUED, EMBL-E	ST58, PIR60, SWISS-
C. DOC	UMENTS CONSIDERED TO BE RELEVANT			
Category*	Citation of document, with indication, where app	propriate, o	of the relevant passages	Relevant to claim No.
x 0	Database EMBASE EST-58, Acces g2183488, HILLIER et al., 'aa12e01.r' sapiens cDNA clone IMAGE:813048 5 PTR5 repetitive element; mRNA seque	l Soares	-NhHMPu-S1 Homo r to contains element	1-11
X	Database EMBASE EST 158, Acce g2887308, PEARCE, A., 'Human DNA on chromosome 1q24. Contains ESTs.'	A seque	nce from PAC 313L4	44-45
Furth	ner documents are listed in the continuation of Box C.	. 🔲	See patent family annex.	
• Sp	ecial categories of cited documents:	*T*,	later document published after the int date and not in conflict with the app	
	cument defining the general state of the art which is not considered be of particular relevance		the principle or theory underlying the	invention
1	rlier document published on or after the international filing date	•x•	document of particular relevance; the considered novel or cannot be consider when the document is taken alone	
cit	cument which may throw doubts on priority claim(s) or which is ad to establish the publication date of another citation or other sois! reason (as specified)	·Y•	document of particular relevance; th	e claimed invention cannot be
*O* do	cument referring to an oral disclosure, use, exhibition or other		considered to involve an inventive combined with one or more other suc being obvious to a person skilled in	step when the document is h documents, such combination
	cument published prior to the international filing date but later than	·a•	document member of the same pater	t family
	actual completion of the international search		nailing of the international sec	arch report
16 NOVE	MBER 1999	1	1 JAN 2000	
Commission Box PCT	mailing address of the ISA/US oner of Patents and Trademarks n, D.C. 20231 No. (703) 305-3230	Authorize NIRI Telephon	nal s. basi	Jolan go
I . acsimile i		1 . 2.2bo	()	. 1/1

International application No. PCT/US99/19351

Box I Chservations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Claims Nos.:  because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
Please See Extra Sheet.
<del>.</del>
1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. X As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:  1-11 and 44-45
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.

International application No. PCT/US99/19351

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s)1-11, drawn to polynucleotide comprising SEQ ID NO:1, fragments thereof, expression vector containing said sequence, cell transformed with said vector, polypeptide of SEQ ID NO:2, fragments of the polypeptide of SEQ ID NO:2 and process for preparing said polypeptide.

Group II, claim(s)12-13, drawn to polynucleotide comprising SEQ ID NO:3, fragments thereof, polypeptide of SEQ ID NO:4 and fragments of the polypeptide of said polypeptide.

Group III, claim(s)14-15, drawn to polynucleotide comprising SEQ ID NO:5, fragments thereof, polypeptide of SEQ ID NO:6 and fragments of the polypeptide of said polypeptide.

Group IV, claim(s)16-17, drawn to polynucleotide comprising SEQ ID NO:7, fragments thereof, polypeptide of SEQ ID NO:8 and fragments of the polypeptide of said polypeptide.

Group V, claim(s)18-19, drawn to polynucleotide comprising SEQ ID NO:9, fragments thereof, polypeptide of SEQ ID NO:10 and fragments of the polypeptide of said polypeptide.

Group VI, claim(s)20-21, drawn to polynucleotide comprising SEQ ID NO:11, fragments thereof, polypeptide of SEQ ID NO:12 and fragments of the polypeptide of said polypeptide.

Group VII, claim(s)22-23, drawn to polynucleotide comprising SEQ ID NO:13, fragments thereof, polypeptide of SEQ ID NO:14 and fragments of the polypeptide of said polypeptide.

Group VIII, claim(s)24-25, drawn to polynucleotide comprising SEQ ID NO:15, fragments thereof, polypeptide of SEQ ID NO:16 and fragments of the polypeptide of said polypeptide.

Group IX, claim(s)26-27, drawn to polynucleotide comprising SEQ ID NO:17, fragments thereof, polypeptide of SEQ ID NO:18 and fragments of the polypeptide of said polypeptide.

Group X, claim(s)28-29, drawn to polynucleotide comprising SEQ ID NO:19, fragments thereof, polypeptide of SEQ ID NO:20 and fragments of the polypeptide of said polypeptide.

Group XI, claim(s)30-31, drawn to polynucleotide comprising SEQ ID NO:21, fragments thereof, polypeptide of SEQ ID NO:22 and fragments of the polypeptide of said polypeptide.

Group XII, claim(s)32-33, drawn to polynucleotide comprising SEQ ID NO:23, fragments thereof, polypeptide of SEQ ID NO:24 and fragments of the polypeptide of said polypeptide.

Group XIII, claim(s)34-35, drawn to polynucleotide comprising SEQ ID NO:25, fragments thereof, polypeptide of SEQ ID NO:26 and fragments of the polypeptide of said polypeptide.

Group XIV, claim(s)36-37, drawn to polynucleotide comprising SEQ ID NO:27, fragments thereof, polypeptide of SEQ ID NO:28 and fragments of the polypeptide of said polypeptide.

Group XV, claim(s)38-39, drawn to polynucleotide comprising SEQ ID NO:29, fragments thereof, polypeptide of SEQ ID NO:30 and fragments of the polypeptide of said polypeptide.

Group XVI, claim(s)40-41, drawn to polynucleotide comprising SEQ ID NO:31, fragments thereof, polypeptide of SEQ ID NO:32 and fragments of the polypeptide of said polypeptide.

Group XVII, claim(s)42-43, drawn to polynucleotide comprising SEQ ID NO:33, fragments thereof, polypeptide of SEQ ID NO:34 and fragments of the polypeptide of said polypeptide.

Group XVIII, claim(s)44-45, drawn to polynucleotide comprising SEQ ID NO:35, fragments thereof, polypeptide of SEQ ID NO:36 and fragments of the polypeptide of said polypeptide.

International application No. PCT/US99/19351

Group XIX, claim(s)46-47, drawn to polynucleotide comprising SEQ ID NO:37, fragments thereof, polypeptide of SEQ ID NO:38 and fragments of the polypeptide of said polypeptide.

Group XX, claim(s)48-49, drawn to polynucleotide comprising SEQ ID NO:39, fragments thereof, polypeptide of SEQ ID NO:40 and fragments of the polypeptide of said polypeptide.

Group XXI, claim(s)50-51, drawn to polynucleotide comprising SEQ ID NO:41, fragments thereof, polypeptide of SEQ ID NO:42 and fragments of the polypeptide of said polypeptide.

Group XXII, claim(s)52-53, drawn to polynucleotide comprising SEQ ID NO:43, fragments thereof, polypeptide of SEQ ID NO:44 and fragments of the polypeptide of said polypeptide.

Group XXIII, claim(s)54-55, drawn to polynucleotide comprising SEQ ID NO:45, fragments thereof, polypeptide of SEQ ID NO:46 and fragments of the polypeptide of said polypeptide.

Group XXIV, claim(s)56-57, drawn to polynucleotide comprising SEQ ID NO:47, fragments thereof, polypeptide of SEQ ID NO:48 and fragments of the polypeptide of said polypeptide.

Group XXV, claim(s)58-59, drawn to polynucleotide comprising SEQ ID NO:49, fragments thereof, polypeptide of SEQ ID NO:50 and fragments of the polypeptide of said polypeptide.

Group XXVI, claim(s)60-61, drawn to polynucleotide comprising SEQ ID NO:51, fragments thereof, polypeptide of SEQ ID NO:52 and fragments of the polypeptide of said polypeptide.

Group XXVII, claim(s)62-63, drawn to polynucleotide comprising SEQ ID NO:53, fragments thereof, polypeptide of SEQ ID NO:54 and fragments of the polypeptide of said polypeptide.

Group XXVIII, claim(s)64-65, drawn to polynucleotide comprising SEQ ID NO:55, fragments thereof, polypeptide of SEQ ID NO:56 and fragments of the polypeptide of said polypeptide.

Group XXIX, claim(s)66-67, drawn to polynucleotide comprising SEQ ID NO:57, fragments thereof, polypeptide of SEQ ID NO:58 and fragments of the polypeptide of said polypeptide.

Group XXX, claim(s)68-69, drawn to polynucleotide comprising SEQ ID NO:59, fragments thereof, polypeptide of SEQ ID NO:60 and fragments of the polypeptide of said polypeptide.

Group XXXI, claim(s)70-71, drawn to polynucleotide comprising SEQ ID NO:61, fragments thereof, polypeptide of SEQ ID NO:62 and fragments of the polypeptide of said polypeptide.

Group XXXII, claim(s)72-73, drawn to polynucleotide comprising SEQ ID NO:63, fragments thereof, polypeptide of SEQ ID NO:64 and fragments of the polypeptide of said polypeptide.

Group XXXIII, claim(s)74-75, drawn to polynucleotide comprising SEQ ID NO:65, fragments thereof, polypeptide of SEQ ID NO:66 and fragments of the polypeptide of said polypeptide.

Group XXXIV, claim(s)76-77, drawn to polynucleotide comprising SEQ ID NO:67, fragments thereof, polypeptide of SEQ ID NO:68 and fragments of the polypeptide of said polypeptide.

Group XXXV, claim(s)78-79, drawn to polynucleotide comprising SEQ ID NO:69, fragments thereof, polypeptide of SEQ ID NO:70 and fragments of the polypeptide of said polypeptide.

Group XXXVI, claim(s)80-81, drawn to polynucleotide comprising SEQ ID NO:71, fragments thereof, polypeptide of SEQ ID NO:72 and fragments of the polypeptide of said polypeptide.

Group XXXVII, claim(s)82-83, drawn to polynucleotide comprising SEQ ID NO:73, fragments thereof, polypeptide of SEQ ID NO:74 and fragments of the polypeptide of said polypeptide.

Group XXXVIII, claim(s)84-85, drawn to polynucleotide comprising SEQ ID NO:75, fragments thereof, polypeptide of SEQ ID NO:76 and fragments of the polypeptide of said polypeptide.

Group XXXIX, claim(s)86-87, drawn to polynucleotide comprising SEQ ID NO:77, fragments thereof, polypeptide of

International application No. PCT/US99/19351

SEQ ID NO:78 and fragments of the polypeptide of said polypeptide.

Group XL, claim(s)88-89, drawn to polynucleotide comprising SEQ ID NO:79, fragments thereof, polypeptide of SEQ ID NO:80 and fragments of the polypeptide of said polypeptide.

The inventions listed as Groups I-XL do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The main invention is Group I, which is first product, first method of making the product and first method of using the product. Pursuant to 37 CFR 1.474 (d), these claims are considered by the ISA/US to constitute the main invention. The products of Groups II-XL do not share the same or corresponding special technical feature with group I because they are drawn to products having materially different structures and functions, each defines a separate invention over the art. Therefore, the claims are not linked by a special technical feature within the meaning of PCT Rule 13.2 so as to form a single inventive concept.